



A 64-year-old man comes to the emergency department due to 2 days of abrupt-onset fever, malaise, and myalgia. He has also had nasal discharge, sore throat, and a nonproductive cough. The patient has a history of hypertension and chronic obstructive pulmonary disease. He is a former smoker but does not use alcohol or illicit drugs. Temperature is 38.3 C (101 F), blood pressure is 130/70 mm Hg, pulse is 96/min, and respirations are 18/min. Physical examination shows watery nasal discharge, pharyngeal erythema, and clear lungs on auscultation. Droplet precautions are immediately instituted to prevent spread of the infection. Hand hygiene with an alcohol-based disinfectant following patient contact is also initiated. This patient's infecting pathogen is likely susceptible to the disinfectant due to the presence of which of the following characteristics?

- ☐ A. Lipid bilayer envelope
- ☐ B. Nucleocapsid proteins
- ☐ C. Segmented RNA genome
- ☐ D. Surface glycoproteins
- ☐ E. Surface ion channels





history of hypertension and chronic obstructive pulmonary disease. He is a former smoker but does not use alcohol or illicit drugs. Temperature is 38.3 C (101 F), blood pressure is 130/70 mm Hg, pulse is 96/min, and respirations are 18/min. Physical examination shows watery nasal discharge, pharyngeal erythema, and clear lungs on auscultation. Droplet precautions are immediately instituted to prevent spread of the infection. Hand hygiene with an alcohol-based disinfectant following patient contact is also initiated. This patient's infecting pathogen is likely susceptible to the disinfectant due to the presence of which of the following characteristics?



- ☒ A. Lipid bilayer envelope (58%)
- ☐ B. Nucleocapsid proteins (10%)
- ☐ C. Segmented RNA genome (5%)
- ☐ D. Surface glycoproteins (17%)
- ☐ E. Surface ion channels (8%)

Correct



58%



01 min, 28 secs

Time Spent



11/28/2020

Last Updated

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Although both **influenza** and the common cold can be associated with upper respiratory symptoms (eg, rhinorrhea, cough, sore throat), influenza can often be differentiated based on the **abrupt onset** of symptoms and the presence of nonspecific, **systemic manifestations** (eg, fever, malaise, myalgias, headache).

The influenza virus is an enveloped orthomyxovirus with a segmented, negative-sense, single-stranded RNA genome. Transmission occurs via contaminated, large-particle droplets. Therefore, patients who are hospitalized with influenza generally require droplet precautions (mask and gown for health care providers), and close contacts should be advised to practice appropriate hand hygiene.

**Alcohol-based disinfectants**, which are composed of ethyl or isopropyl alcohol (at concentrations of 60%-90%) in water, are often used for hand hygiene. These solutions kill vegetative bacteria (but not spores), fungus, and **enveloped viruses** (eg, influenza, HIV, herpes) by **dissolving their lipid bilayer membranes** and subsequently denaturing their proteins. Nonenveloped viruses such as adenovirus, rhinovirus, enterovirus, and poliovirus are less susceptible to some alcohol-based disinfectants (particularly isopropyl-based solutions) because they do not have a lipid bilayer envelope.

**(Choice B)** Proteins (and spores) are sterilized by moist heat (eg, autoclave), which results in protein denaturation. Although proteins are somewhat susceptible to alcohol-based disinfectants, high





isopropyl-based solutions) because they do not have a lipid bilayer envelope.

**(Choice B)** Proteins (and spores) are sterilized by moist heat (eg, autoclave), which results in protein denaturation. Although proteins are somewhat susceptible to alcohol-based disinfectants, high concentrations must be used and efficacy is variable. Alcohol has the strongest effect on lipophilic membranes.

**(Choice C)** RNA can be rendered inert by ionizing radiation, which dislodges electrons and results in the formation of reactive ions that break covalent bonds. Alcohol has a minimal effect on RNA molecule integrity.

**(Choice D)** Neuraminidase, 1 of the 2 influenza surface glycoproteins, can be blocked by neuraminidase inhibitors (eg, oseltamivir, zanamivir). These are often used to treat acute influenza (prevent the virus from leaving infected cells).

**(Choice E)** The M2 ion channel mediates fusion of the influenza envelope with the endosome membrane, which liberates the influenza nucleocapsid and enzymes into the cytoplasm of the host cells. Blockade of the M2 ion channel with amantadine can prevent influenza infection. However, because influenza virus has developed widespread resistance to M2 ion channel inhibitors, these drugs are not recommended for use in the United States.







**(Choice D)** Neuraminidase, 1 of the 2 influenza surface glycoproteins, can be blocked by neuraminidase inhibitors (eg, oseltamivir, zanamivir). These are often used to treat acute influenza (prevent the virus from leaving infected cells).

**(Choice E)** The M2 ion channel mediates fusion of the influenza envelope with the endosome membrane, which liberates the influenza nucleocapsid and enzymes into the cytoplasm of the host cells. Blockade of the M2 ion channel with amantadine can prevent influenza infection. However, because influenza virus has developed widespread resistance to M2 ion channel inhibitors, these drugs are not recommended for use in the United States.

**Educational objective:**

Alcohol-based disinfectants kill enveloped viruses (eg, influenza) by dissolving their outer lipid envelope. Nonenveloped viruses are less susceptible to some alcohol-based disinfectants because they have no lipid envelope to target.

Microbiology

Subject

Microbiology (General Principles)

System

Influenza

Topic

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A 34-year-old woman comes to the physician complaining of fever, dysuria, and flank pain. Her temperature is 37.8 C (100 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. Physical examination elicits suprapubic and costovertebral angle tenderness. Urine dipstick analysis reveals positive leukocyte esterase and nitrite. A subsequent urine culture grows colonies of motile Gram-negative rods demonstrating a green metallic sheen on eosin methylene blue (EMB) agar and hemolysis on blood agar. Which of the following is the most important bacterial factor responsible for this patient's condition?

- ☐ A. Capsule
- ☐ B. Heat-labile enterotoxin
- ☐ C. O antigen
- ☐ D. Fimbrial antigen
- ☐ E. Lipid A

**Submit**



A 34-year-old woman comes to the physician complaining of fever, dysuria, and flank pain. Her temperature is 37.8 C (100 F), blood pressure is 122/78 mm Hg, and pulse is 84/min. Physical examination elicits suprapubic and costovertebral angle tenderness. Urine dipstick analysis reveals positive leukocyte esterase and nitrite. A subsequent urine culture grows colonies of motile Gram-negative rods demonstrating a green metallic sheen on eosin methylene blue (EMB) agar and hemolysis on blood agar. Which of the following is the most important bacterial factor responsible for this patient's condition?

- ☐ A. Capsule (14%)
- ☐ B. Heat-labile enterotoxin (6%)
- ☐ C. O antigen (6%)
- ☒ D. Fimbrial antigen (59%)
- ☐ E. Lipid A (12%)

Correct



59%

Answered correctly



33 secs

Time Spent



01/02/2021

Last Updated

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Previous



Next



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Tutorial



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Notes



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### *Escherichia coli* virulence factors

Virulence factor	Mechanism	Presentation
<b>Lipopolysaccharide</b>	Macrophage activation causes widespread release of IL-1, IL-6 & TNF- $\alpha$	Bacteriemia & septic shock
<b>K1 capsular polysaccharide</b>	Prevents phagocytosis & complement-mediated lysis	Neonatal meningitis
<b>Verotoxin (shiga-like toxin)</b>	Inactivates the 60S ribosomal component, halting protein synthesis & causing cell death	Gastroenteritis (bloody)
<b>Heat-stable/heat-labile enterotoxins</b>	Promotes fluid & electrolyte secretion from intestinal epithelium	Gastroenteritis (watery)
<b>P fimbriae</b>	Allows adhesion to uroepithelium	Urinary tract infections

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*Escherichia coli* is part of the normal bacterial flora of the intestinal tract. It is a motile, Gram-negative

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*Escherichia coli* is part of the normal bacterial flora of the intestinal tract. It is a motile, Gram-negative bacillus that is facultatively anaerobic and able to ferment both lactose and glucose. *E coli* grows well on blood, MacConkey, and eosin methylene blue (EMB) agar plates. EMB agar is a selective and differential medium used to isolate and identify enteric pathogens from contaminated clinical specimens. On EMB agar, organisms that ferment lactose, such as *E coli*, bind to dye in the agar and produce colonies that have a distinct green metallic sheen. Most strains of *E coli* also demonstrate beta-hemolysis on blood agar.

*E coli* is responsible for urinary tract infections (UTIs), neonatal meningitis, and several types of gastroenteritis. The virulence factors expressed by a particular strain of *E coli* will determine disease characteristics. **Fimbriae**, or **pili** (Type 1 fimbriae, P fimbriae, and S fimbriae), are one of the most important virulence factors expressed by *E coli*. They permit the adhesion of *E coli* to epithelial cells, uroepithelial cells, and enterocytes.

*E coli* causes approximately 80% of all UTIs. UTIs are more common in women than men due to the female urethra being significantly shorter. *E coli* originates in the feces and spreads to colonize the perineal, genital, and – most importantly – the periurethral regions. During sexual intercourse or bladder catheterization, *E coli* can be propelled into the urethra and bladder from the colonized periurethral region.



P-fimbriae (pyelonephritis-associated pili) adhesion then allows uropathogenic *E coli* to colonize the bladder and ureters, causing cystitis and pyelonephritis.

**(Choice A)** *E coli* strains causing neonatal meningitis synthesize K1 capsular antigens. The K1 antigen is considered the major determinant of virulence among strains of *E coli* that cause meningitis.

**(Choice B)** Enterotoxigenic *E coli* produce heat-stable (ST) and/or heat labile (LT) enterotoxins. ST activates guanylate cyclase, causing an increase in cGMP. LT activates adenylate cyclase, increasing cAMP levels. In both structure and mode of action, LT is very similar to the cholera toxin.

**(Choice C)** The O antigen is a variable polysaccharide antigen found on the outer membrane that is used to classify Gram-negative bacteria. It is the most extracellular component of lipopolysaccharide (see Choice E).

**(Choice E)** The lipid A component of lipopolysaccharide is similar for all enterobacteria. Lipid A causes activation of macrophages, leading to widespread release of IL-1, IL-6, and TNF-alpha, which in turn causes the signs and symptoms of septic shock.

**Educational objective:**

*E coli* is one of the dominant components of the normal flora in the intestinal tract of humans and animals.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

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considered the major determinant of virulence among strains of *E. coli* that cause meningitis.

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**(Choice C)** The O antigen is a variable polysaccharide antigen found on the outer membrane that is used to classify Gram-negative bacteria. It is the most extracellular component of lipopolysaccharide (see Choice E).

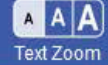
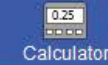
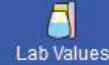
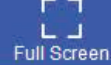
**(Choice E)** The lipid A component of lipopolysaccharide is similar for all enterobacteria. Lipid A causes activation of macrophages, leading to widespread release of IL-1, IL-6, and TNF-alpha, which in turn causes the signs and symptoms of septic shock.

### Educational objective:

*E. coli* is one of the dominant components of the normal flora in the intestinal tract of humans and animals. It causes approximately 80% of all urinary tract infections. P fimbriae are the most important virulence factor that uropathogenic *E. coli* express. Without P fimbriae, *E. coli* would not be able to bind to uroepithelial cells and infect the bladder, ureters, and kidneys. Instead, the bacteria would simply be washed away during urination.



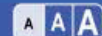




Microbiologists are investigating sugar metabolism in wild-type and mutant strains of *Escherichia coli*. Both strains are found to grow viable colonies on lactose-containing media. Each strain is then cultured on a new growth medium containing only glucose. Representative colonies of each strain from the new media undergo Western blot processing using a fluorescently labeled probe specific for  $\beta$ -galactosidase. Wild-type bacterial colonies are found to contain only trace quantities of  $\beta$ -galactosidase. However, the mutant colonies express significant amounts of  $\beta$ -galactosidase. Further analysis reveals that the variant strain contains a mutation that inhibits the binding of a certain protein to its regulatory sequence. In which of the following locations did this mutation most likely occur?

- ☐ A. Activator protein (CAP) binding site
- ☐ B. Operator locus
- ☐ C. Promoter region
- ☐ D. Activator protein (CAP) gene
- ☐ E. RNA polymerase cistron





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- ☐ A. Activator protein (CAP) binding site (19%)
- ☒ B. Operator locus (43%)
- ☐ C. Promoter region (27%)
- ☐ D. Activator protein (CAP) gene (8%)
- ☐ E. RNA polymerase cistron (1%)

Correct

43%



02 mins, 31 secs



02/01/2021

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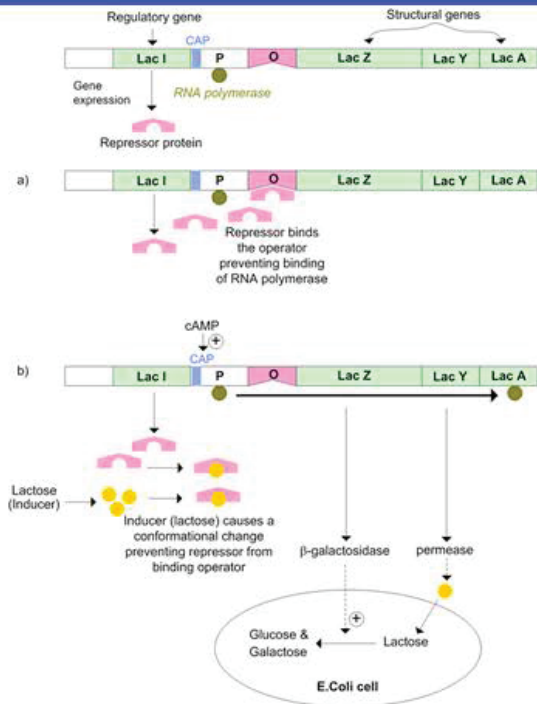
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## E.Coli cell

The *lac* operon consists of a regulatory gene (*lac I*), a promoter region (*lac p*), an operator region (*lac o*), and three structural genes (*lac Z*, *lac Y*, and *lac A*). The *lac Z* gene codes for  $\beta$ -galactosidase, which is responsible for the hydrolysis of lactose to glucose and galactose. The *lac Y* gene codes for permease, which allows lactose to enter the bacterium. The *lac p* region is the binding site for RNA polymerase during the initiation of transcription. The Lac I repressor protein is the product of the *lac I* gene and is constitutively expressed. Repressor proteins, when bound to the operator region, prevent binding of RNA polymerase to the promoter region, thus decreasing transcription of the *lac Z*, *lac Y*, and *lac A* genes. Culture of *E coli* in lactose-containing media causes a conformational change in the repressor protein, preventing its attachment to the operator region and increasing transcription of the *lac* operon structural genes.

Culturing *E coli* in media containing glucose results in reduced expression of the *lac* operon, even when the media contains lactose as well. This occurs because the *lac* operon is positively regulated by the binding of catabolite activator protein (CAP) to a site slightly upstream from the promoter region. This only occurs when cAMP concentrations are high. Since glucose decreases the activity of adenylyl cyclase (reducing intracellular cAMP), the *lac* operon is repressed in high-glucose conditions. In summary, the *lac* operon is





or catabolite activator protein (CAP) to a site slightly upstream from the promoter region. This only occurs when cAMP concentrations are high. Since glucose decreases the activity of adenyl cyclase (reducing intracellular cAMP), the *lac* operon is repressed in high-glucose conditions. In summary, the *lac* operon is regulated by 2 distinct mechanisms:

1. Negatively by binding of the repressor protein to the operator locus
2. Positively by cAMP-CAP binding upstream from the promoter region

Mutations impairing the binding of the repressor protein to its binding site at the operator region will prevent repression of the genes of the *lac* operon in the absence of lactose. This results in increased transcription of the genes of the *lac* operon in lactose-deficient media, although the presence of glucose will prevent maximal transcriptional activity.

**(Choices A and D)** Mutations that impair the binding of cAMP-CAP to its regulatory site upstream from the promoter will decrease transcription of the *lac* operon, as cAMP-CAP is a positive regulator.

**(Choices C and E)** Mutations impairing the binding of RNA polymerase to the promoter region will also reduce transcription of the *lac* operon.

### Educational objective:

The *lac* operon is regulated by two distinct mechanisms: negatively by binding of the repressor protein to





Mutations impairing the binding of the repressor protein to its binding site at the operator region will prevent repression of the genes of the *lac* operon in the absence of lactose. This results in increased transcription of the genes of the *lac* operon in lactose-deficient media, although the presence of glucose will prevent maximal transcriptional activity.

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**(Choices C and E)** Mutations impairing the binding of RNA polymerase to the promoter region will also reduce transcription of the *lac* operon.

### Educational objective:

The *lac* operon is regulated by two distinct mechanisms: negatively by binding of the repressor protein to the operator locus and positively by cAMP-CAP binding upstream from the promoter region. Constitutive expression of the structural genes of the *lac* operon occurs with mutations that impair the binding of the repressor protein (Lac I) to its regulatory sequence in the operator region.

Microbiology

Microbiology (General Principles)

Lac operon

Subject

System

Topic

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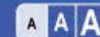




A 45-year-old woman comes to the emergency department due to 2 days of fever, chills, malaise, and fatigue. The patient returned from an African jungle safari 3 weeks ago. She received mefloquine chemoprophylaxis during the travel, which she stopped taking upon arrival in the United States. Temperature is 38.9 C (102 F), blood pressure is 122/68 mm Hg, pulse is 110/min, and respirations are 20/min. Physical examination shows mucosal pallor. Laboratory results reveal mild anemia and thrombocytopenia. Peripheral blood smear shows intraerythrocytic *Plasmodium falciparum*. Which of the following is the most likely underlying cause of this patient's infection?

- ☐ A. Inactivity of mefloquine against gametocytes
- ☐ B. Infection with parasites resistant to chloroquine
- ☐ C. Mosquito bite after discontinuation of prophylaxis
- ☐ D. Impaired clearance of liver schizonts
- ☐ E. Release of dormant hypnozoites from hepatocytes

**Submit**



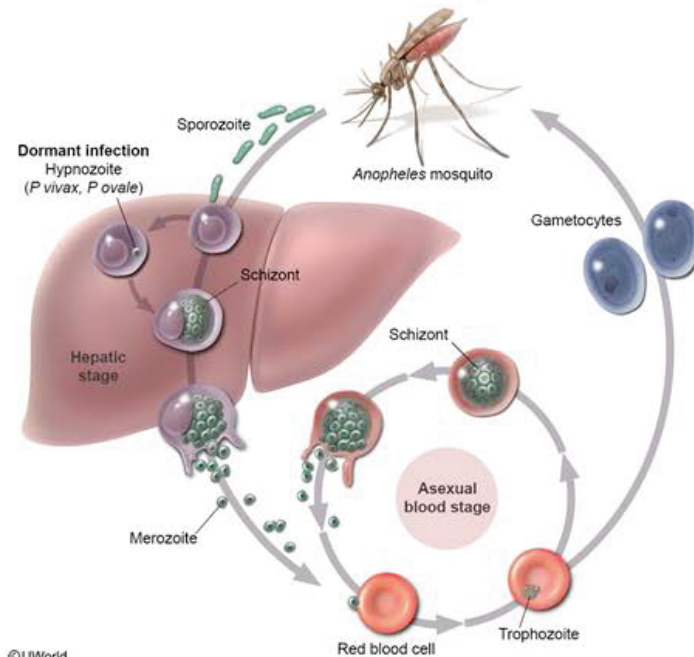
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- ☐ A. Inactivity of mefloquine against gametocytes (13%)
- ☐ B. Infection with parasites resistant to chloroquine (27%)
- ☐ C. Mosquito bite after discontinuation of prophylaxis (3%)
- ☒ D. Impaired clearance of liver schizonts (20%)
- ☐ E. Release of dormant hypnozoites from hepatocytes (34%)



## Exhibit Display

## Malaria life cycle



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Travelers to **malaria-endemic regions** should be counseled on mosquito avoidance measures and given chemoprophylaxis. **Mosquito avoidance** strategies include staying indoors at dawn/dusk (when mosquitos are most active), wearing insect repellant, limiting exposed skin, and sleeping within insecticide-treated nets. **Chemoprophylaxis** targets the predominant species of the region and takes into account the presence of drug resistance. In Africa, where chloroquine-resistant *Plasmodium falciparum* is endemic, common chemoprophylaxis regimens include atovaquone-proguanil, doxycycline, and mefloquine.

**Mefloquine** is a schizonticide that actively **destroys replicating parasites** within red blood cells. However, it is inactivated in the liver and has **no efficacy against hepatic schizonts**. Therefore, patients must receive mefloquine chemoprophylaxis for **4 weeks upon return** to ensure that parasites released from the liver are destroyed when they infect red blood cells (liver schizonts rupture over 8-30 days). Individuals who do not take mefloquine upon return (as in this case) are at risk for hepatic schizont release and subsequent red cell infection, leading to symptomatic malaria.

**(Choice A)** Malaria undergoes asexual reproduction in humans. However, a minority of circulating merozoites differentiate into male and female gametocytes that can be passed to feeding *Anopheles* mosquitos to continue their replicative cycle (malaria undergoes sexual reproduction in the midgut of the mosquito). Gametocytes do not undergo sexual reproduction in humans and do not cause symptoms.





Item 4 of 31

Question Id: 15453



Mark



Previous



Next



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Lab Values



Notes



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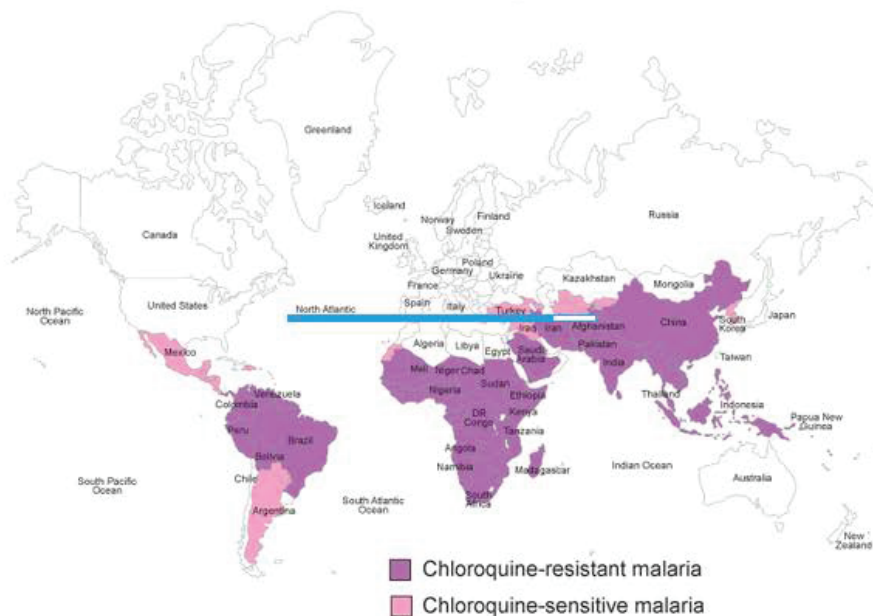
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## Exhibit Display

## Map of malaria regions



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mosquito). Gametocytes do not undergo sexual reproduction in humans and do not cause symptoms.

**(Choice B)** Cases of *P falciparum* in Africa are usually resistant to chloroquine. Therefore, alternate agents (eg, mefloquine) are given for chemoprophylaxis. Cross-resistance between classes of medications does not typically occur.

**(Choice C)** Malaria has been eradicated from the United States; therefore, individuals who develop malaria in the United States were infected while in other countries. This patient continued prophylaxis during the duration of her travels but ceased prophylaxis upon her return, which allowed developing hepatic schizonts to infect red blood cells and cause malaria.

**(Choice E)** *P ovale* and *P vivax* have a dormant hepatic phase (hypnozoite) that may reactivate several months after return from an endemic region (if not treated with primaquine). In contrast, *P falciparum* does not have a dormant hepatic phase; it matures in (and is released from) the liver over 8-30 days.

### Educational objective:

Mefloquine chemoprophylaxis for malaria must be continued for 4 weeks after return from an endemic region to ensure the elimination of hepatic schizonts (which develop in the liver over 8-30 days).

Microbiology      Microbiology (General Principles)      Malaria  
 Subject              System                              Topic





A 26-year-old man comes to the office due to a 3-day-history of dysuria and urethral discharge. The symptoms developed about 2 weeks after he had unprotected sexual intercourse with a new partner. His temperature is 37.1 C (98.8 F). On physical examination, a mucoid discharge is expressed with gentle milking of the penis. Gram stain of the discharge reveals numerous neutrophils with intracellular diplococci. A sample of the discharge is placed on an antibiotic-containing medium, and bacterial colonies are cultured. Which of the following terms best describes the medium?

- ☐ A. Differential
- ☐ B. Enrichment
- ☐ C. Reducing
- ☐ D. Selective
- ☐ E. Synthetic

**Submit**



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- ☐ A. Differential (5%)
- ☐ B. Enrichment (7%)
- ☐ C. Reducing (2%)
- ☒ D. Selective (83%)
- ☐ E. Synthetic (0%)

Correct



83%

Answered correctly



52 secs

Time Spent



01/25/2021

Last Updated

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This patient with dysuria and urethral discharge has **gonococcal urethritis** as indicated by the Gram stain showing gram-negative diplococci within leukocytes. *Neisseria gonorrhoeae* can be cultured on Thayer-Martin VCN **selective** medium, which contains vancomycin, colistin, nystatin, and trimethoprim. These antibiotics kill potential contaminants such as gram-positive organisms (vancomycin), gram-negative organisms other than *Neisseria* (colistin and trimethoprim), and fungi (nystatin).

**(Choice A)** Differential media help identify cultured organisms based on their metabolic and biochemical properties. Examples of differential media include the MacConkey and eosin methylene blue (EMB) agars used to culture enteric organisms. Organisms that ferment lactose will appear pink on MacConkey agar and black on EMB agar.

**(Choice B)** Enrichment media contain special growth factors required for some organisms. Examples include the X and V factors required by *Haemophilus* or the anaerobic conditions needed by *Clostridium* species.

**(Choice C)** Reducing media (eg, thioglycolate broth) remove oxygen and are used to culture anaerobic organisms.

**(Choice E)** A synthetic medium is any chemically-defined medium for which all of the chemical contents are known.







and black on EMB agar.

**(Choice B)** Enrichment media contain special growth factors required for some organisms. Examples include the X and V factors required by *Haemophilus* or the anaerobic conditions needed by *Clostridium* species.

**(Choice C)** Reducing media (eg, thioglycolate broth) remove oxygen and are used to culture anaerobic organisms.

**(Choice E)** A synthetic medium is any chemically-defined medium for which all of the chemical contents are known.

**Educational objective:**

*Neisseria* can be isolated by culture on selective media such as the Thayer-Martin VCN (vancomycin/colistin/nystatin) medium, which inhibits growth of contaminants such as gram-positive organisms, gram-negative organisms other than *Neisseria*, and fungi.

Microbiology  
Subject

Microbiology (General Principles)  
System

Urethritis  
Topic

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A 45-year-old man comes to the physician due to pain, swelling, and erythema affecting his right leg. He says that he suffered a minor cut to his leg a few days ago while cleaning his garage. Physical examination shows an indurated region surrounding a minor laceration that is draining a purulent exudate. He is diagnosed with cellulitis and started on the appropriate treatment. Gram stain of the exudate shows gram-positive cocci in clusters. The organism most likely responsible for this patient's infection synthesizes a protein as part of its peptidoglycan cell wall that does which of the following?

- ☐ A. Activates complement
- ☐ B. Binds the Fc portion of IgG
- ☐ C. Causes hemolysis
- ☐ D. Cleaves IgA
- ☐ E. Interacts with MHC class II antigens

**Submit**



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- ☐ A. Activates complement (8%)
- ☒ B. Binds the Fc portion of IgG (56%)
- ☐ C. Causes hemolysis (11%)
- ☐ D. Cleaves IgA (15%)
- ☐ E. Interacts with MHC class II antigens (8%)

Correct



56%  
Answered correctly



01 min, 09 secs  
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12/09/2020  
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Feedback



Suspend

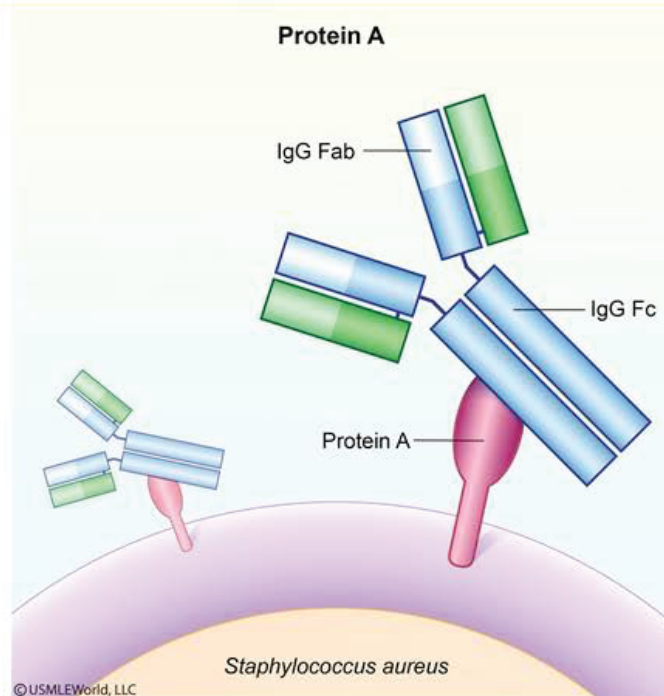


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## Exhibit Display



Zoom In



Zoom Out



Reset



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Clusters of gram-positive cocci on Gram stain is a characteristic finding of staphylococcal species such as *Staphylococcus aureus*. Protein A is a virulence factor that forms part of the outer peptidoglycan layer of *S. aureus*. Protein A binds with the Fc portion of IgG antibodies at the complement-binding site, preventing complement activation (**Choice A**). This results in decreased production of C3b, leading to impaired opsonization and phagocytosis.

(**Choice C**) Hemolysin is secreted by staphylococci and causes hemolysis as well as the destruction of neutrophils, macrophages, and platelets. It is a secreted factor that is not bound to the cell wall.

(**Choice D**) *Streptococcus pneumoniae* and *Neisseria gonorrhoeae* produce IgA proteases that cause cleavage of IgA antibodies, preventing them from interfering with bacterial adhesion to mucous membranes.

(**Choice E**) Major histocompatibility complex (MHC) class II (found on an antigen presenting cells) normally interacts with processed antigens, presenting them to T-lymphocytes to initiate an immune response. In contrast, superantigens (enterotoxins, toxic shock syndrome toxin) interact with MHC class II and the T-cell receptor outside of standard antigen binding sites to initiate widespread and nonspecific activation of T- lymphocytes. Although superantigens are synthesized by staphylococci, they are not bound to the peptidoglycan cell wall.



**(Choice D)** *Streptococcus pneumoniae* and *Neisseria gonorrhoeae* produce IgA proteases that cause cleavage of IgA antibodies, preventing them from interfering with bacterial adhesion to mucous membranes.

**(Choice E)** Major histocompatibility complex (MHC) class II (found on an antigen presenting cells) normally interacts with processed antigens, presenting them to T-lymphocytes to initiate an immune response. In contrast, superantigens (enterotoxins, toxic shock syndrome toxin) interact with MHC class II and the T-cell receptor outside of standard antigen binding sites to initiate widespread and nonspecific activation of T- lymphocytes. Although superantigens are synthesized by staphylococci, they are not bound to the peptidoglycan cell wall.

### Educational objective:

Protein A is a virulence factor found in the peptidoglycan cell wall of *Staphylococcus aureus* that binds to the Fc portion of IgG, leading to impaired complement activation, opsonization, and phagocytosis.

Microbiology

Subject

Microbiology (General Principles)

System

Skin and soft tissue infections

Topic

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A 3-week-old baby boy is brought to the emergency department with fever, irritability, and poor feeding. Examination of the cerebrospinal fluid shows a leukocyte count of 600 cells/ $\mu$ L (80% neutrophils), protein of 160 mg/dL, and glucose of 20 mg/dL. Blood cultures grow gram-negative rods that form pink colonies on MacConkey agar. Which of the following is the most important bacterial virulence factor for the development of this patient's condition?

- ☐ A. Capsule
- ☐ B. Fimbrial antigen
- ☐ C. Lipid A
- ☐ D. O antigen
- ☐ E. Verotoxin

Submit





A 3-week-old baby boy is brought to the emergency department with fever, irritability, and poor feeding. Examination of the cerebrospinal fluid shows a leukocyte count of 600 cells/ $\mu$ L (80% neutrophils), protein of 160 mg/dL, and glucose of 20 mg/dL. Blood cultures grow gram-negative rods that form pink colonies on MacConkey agar. Which of the following is the most important bacterial virulence factor for the development of this patient's condition?



☒ A. Capsule (56%)

☐ B. Fimbrial antigen (16%)

☐ C. Lipid A (17%)

☐ D. O antigen (7%)

☐ E. Verotoxin (2%)

Correct



56%

Answered correctly



32 secs

Time Spent



01/02/2021

Last Updated





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

***Escherichia coli* virulence factors**

Virulence factor	Mechanism	Presentation
Lipopolysaccharide	Macrophage activation causes widespread release of IL-1, IL-6 & TNF- $\alpha$	Bacteriemia & septic shock
K1 capsular polysaccharide	Prevents phagocytosis & complement-mediated lysis	Neonatal meningitis
Verotoxin (shiga-like toxin)	Inactivates the 60S ribosomal component, halting protein synthesis & causing cell death	Gastroenteritis (bloody)
Heat-stable/heat-labile enterotoxins	Promotes fluid & electrolyte secretion from intestinal epithelium	Gastroenteritis (watery)
P fimbriae	Allows adhesion to uroepithelium	Urinary tract infections

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End Block





Group B *Streptococcus* is the most common cause of neonatal meningitis (0-3 months) in the United States, followed by *Escherichia coli* and *Listeria monocytogenes*. In older infants (>3 months) and adults, the most common pathogens are *Streptococcus pneumoniae* and *Neisseria meningitidis*.

This patient has meningitis secondary to ***E coli*** infection. *E coli* is a motile, gram-negative, facultative anaerobic rod that is able to ferment both lactose and glucose. It grows well on blood, MacConkey, and eosin methylene blue agar plates. **MacConkey agar** is a selective and differential medium used to isolate gram-negative organisms from contaminants in clinical specimens. The bile salts and crystal violet present in MacConkey agar prevent the growth of gram-positive organisms. Organisms that **ferment lactose** (eg, *E coli*, *Klebsiella*, *Enterobacter*) cause a local drop in pH, resulting in **colonies with a pink-red appearance**. Non-lactose fermenting organisms remain colorless.

*E coli* can invade the blood stream of infants from the nasopharynx or gastrointestinal tract and can then travel hematogenously to the meninges. The **K1 capsular antigen** is present in 20%-40% of intestinal *E coli* isolates and is considered the major virulence factor among *E coli* strains that cause **neonatal meningitis**. Bacterial capsules are important for most meningeal pathogens. They help facilitate survival in the blood by preventing recognition of bacterial antigens, complement deposition, and subsequent



isolates and is considered the major virulence factor among *E. coli* strains that cause neonatal

**meningitis.** Bacterial capsules are important for most meningeal pathogens. They help facilitate survival in the blood by preventing recognition of bacterial antigens, complement deposition, and subsequent phagocytosis. The K1 capsule is immunogenic and anti-capsular antibodies are protective against repeat infection.

**(Choice B)** Fimbriae (pili) are a virulence factor that allows bacteria to adhere to the target tissue, thereby establishing infection. Examples of organisms that use pili are *Neisseria gonorrhoeae*, uropathogenic *E. coli*, and *Vibrio cholerae*.

**(Choice C)** The lipid A unit in lipopolysaccharides is similar for all enteric bacteria; it causes activation of macrophages, leading to widespread release of IL-1 and TNF- $\alpha$ , which in turn cause the signs and symptoms of septic shock.

**(Choice D)** The O antigen is the outermost component of the lipopolysaccharide molecule. It is a variable polysaccharide that can be used to classify gram-negative bacteria.

**(Choice E)** Verotoxin (shiga-like toxin) is synthesized by enterohemorrhagic *E. coli*. Exotoxin expression is not present in any of the pathogens commonly associated with neonatal meningitis.

**Educational objective:**



establishing infection. Examples of organisms that use pili are *Neisseria gonorrhoeae*, uropathogenic *E. coli*, and *Vibrio cholerae*.

**(Choice C)** The lipid A unit in lipopolysaccharides is similar for all enteric bacteria; it causes activation of macrophages, leading to widespread release of IL-1 and TNF- $\alpha$ , which in turn cause the signs and symptoms of septic shock.

**(Choice D)** The O antigen is the outermost component of the lipopolysaccharide molecule. It is a variable polysaccharide that can be used to classify gram-negative bacteria.

**(Choice E)** Verotoxin (shiga-like toxin) is synthesized by enterohemorrhagic *E. coli*. Exotoxin expression is not present in any of the pathogens commonly associated with neonatal meningitis.

### Educational objective:

*Escherichia coli* is a frequent cause of neonatal meningitis, second only to group B streptococci. *E. coli* strains that cause neonatal meningitis possess the K1 capsular antigen. The K1 capsule is a virulence factor that allows the bacteria to survive in the bloodstream and establish meningeal infection.

Microbiology

Microbiology (General Principles)

Neonatal sepsis

Subject

System

Topic





A 52-year-old woman is evaluated due to 2 weeks of fever, fatigue, nonproductive cough, and dyspnea, which began shortly after visiting her family in Ohio. She also lost 1.5 kg (3.3 lb) over the same period. The patient has a history of rheumatoid arthritis and has been taking adalimumab for the past 6 months. She had negative tuberculosis skin testing prior to beginning the drug. Temperature is 38 C (100.4 F), blood pressure is 130/70 mm Hg, pulse is 92/min, and respirations are 18/min. Physical examination reveals bilateral lung crackles, mild generalized lymphadenopathy, and hepatosplenomegaly. Chest x-ray shows bilateral nodular densities and hilar lymphadenopathy. Urine testing is positive for a fungal antigen. Which of the following pathogenic processes is most important during the development of this patient's infection?

- ☐ A. Intracellular proliferation within the macrophages
- ☐ B. Invasion of the vascular endothelial lining
- ☐ C. Overgrowth and tissue invasion by endogenous flora
- ☒ D. Production of an antiphagocytic polysaccharide capsule
- ☐ E. Transformation into a mycelial form in tissues





The patient has a history of rheumatoid arthritis and has been taking **adalimumab** for the past 6 months. She had negative tuberculosis skin testing prior to beginning the drug. Temperature is 38 C (100.4 F), blood pressure is 130/70 mm Hg, pulse is 92/min, and respirations are 18/min. Physical examination reveals bilateral lung crackles, mild generalized **lymphadenopathy**, and **hepatosplenomegaly**. Chest x-ray shows bilateral nodular densities and hilar lymphadenopathy. Urine testing is positive for a fungal antigen. Which of the following pathogenic processes is most important during the development of this patient's infection?

- ☒ A. Intracellular proliferation within the macrophages (70%)
- ☐ B. Invasion of the vascular endothelial lining (6%)
- ☐ C. Overgrowth and tissue invasion by endogenous flora (3%)
- ☐ D. Production of an antiphagocytic polysaccharide capsule (7%)
- ☐ E. Transformation into a mycelial form in tissues (13%)

Correct

70%  
Answered correctly01 min, 08 secs  
Time Spent12/02/2020  
Last Updated

Block Time Remaining: 00:09:07

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2



Feedback



Suspend



End Block



### *Histoplasma capsulatum*

<b>Epidemiology</b>	<ul style="list-style-type: none"><li>• Dimorphic fungus – mold in environment, yeast at body temperature</li><li>• Endemic to Ohio &amp; Mississippi River Valleys</li><li>• Soil contaminated by bird or bat droppings</li></ul>
<b>Pathophysiology</b>	<ul style="list-style-type: none"><li>• Inhaled → phagocytosed by alveolar macrophages → escapes lysosome destruction → spreads to hilar/mediastinal lymph nodes</li><li>• Controlled by cell-mediated immune response (<b>granulomas</b>)</li></ul>
<b>Disease course</b>	<ul style="list-style-type: none"><li>• Immunocompetent: Asymptomatic (primarily) or self-limited pneumonia with mediastinal/hilar lymphadenopathy</li><li>• <b>Immunocompromised</b>: Disseminated disease through liver, spleen, or bone marrow</li></ul>
<b>Diagnosis</b>	<ul style="list-style-type: none"><li>• Urine antigen testing</li><li>• Biopsy with histopathology – granulomas &amp; macrophages with <b>intracellular ovoid/round yeast</b></li></ul>







This patient's rheumatoid arthritis is being treated with adalimumab, a **tumor necrosis factor (TNF)-alpha inhibitor**. TNF-alpha is a crucial cytokine of the cell-mediated immune response that aids in macrophage activation, phagolysosome function, and the formation and maintenance of **granulomas**. Blockade of TNF-alpha **increases the risk of infection** with pathogens controlled by the cell-mediated immune response such as intracellular bacteria (eg, *Mycobacterium tuberculosis*), viruses, and granulomatous fungi.

This patient's pulmonary and reticuloendothelial (eg, lymphadenopathy, splenomegaly) findings and positive urine fungal antigen test raise strong suspicion for infection with ***Histoplasma capsulatum***, a dimorphic fungus endemic to the **Ohio** and Mississippi River Valleys. *H capsulatum* is a mold that is inhaled from contaminated soil and converts to a yeast form in the lungs. Phagocytosis by alveolar macrophages does not result in destruction of the organism due to microbial virulence factors that prevent phagolysosome acidification. Therefore, for the first several weeks of infection, *H capsulatum* is able to **proliferate within macrophages** in an unchecked fashion.

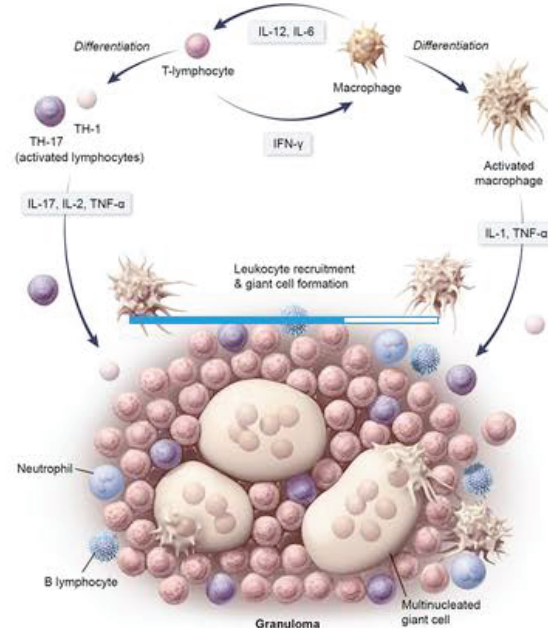
Eventually, the cell-mediated immune response controls the infection in most healthy patients. However, those with impaired immunity (as in this case) are at high risk for life-threatening **disseminated disease**. The lungs, reticuloendothelial system, and mouth (oral ulcers) are most commonly affected. Urine *Histoplasma* antigen testing is often used to quickly confirm the diagnosis.





## Exhibit Display

## Pathogenesis of granulomas



IFN = interferon; TH = T helper; TNF = tumor necrosis factor.

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Zoom In



Zoom Out



Reset



New



Existing

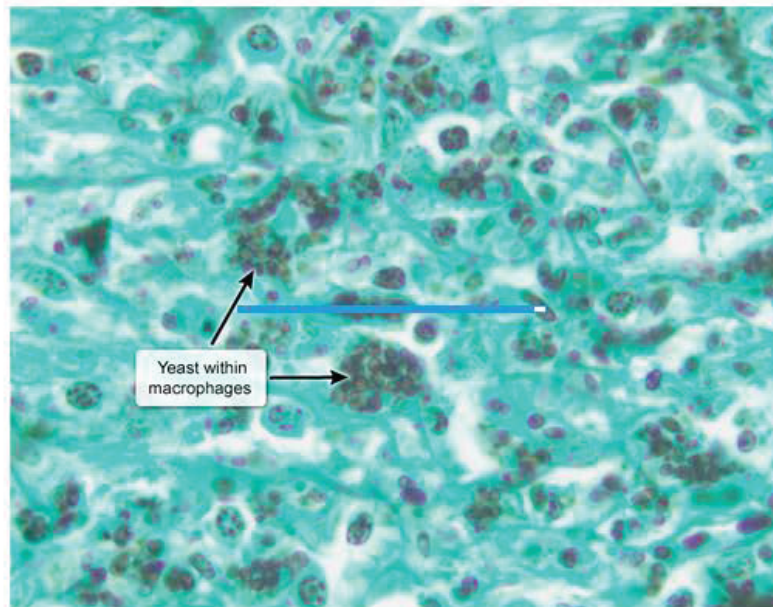


My Notebook





## Exhibit Display

*Histoplasma*Yeast within  
macrophages

Silver stain

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Zoom In



Zoom Out



Reset



New | Existing



My Notebook







*Histoplasma* antigen testing is often used to quickly confirm the diagnosis.

**(Choice B)** *Aspergillus fumigatus* is a monomorphic mold that can cause invasive disease in those who are immunocompromised. This organism is inhaled into the lungs and can invade the vascular endothelial lining, leading to dissemination through the bloodstream. However, patients usually have fever, chest pain, and hemoptysis.

**(Choice C)** *Candida* species are part of the endogenous human flora, but overgrowth can occur in those with immunocompromise and lead to mucocutaneous (eg, thrush) or invasive (pneumonia, fungemia) disease. Invasive *Candida* infections are generally diagnosed by blood culture or biopsy with histopathology, not urine antigen testing.

**(Choice D)** *Cryptococcus neoformans* is a yeast with a thick, antiphagocytic, polysaccharide capsule that primarily causes infections in those who are immunocompromised (particularly patients with advanced AIDS). Although pulmonary infection can occur, disseminated disease is usually marked by meningoencephalitis (eg, headache, confusion, altered mental state).

**(Choice E)** *Malassezia* is a dimorphic fungus that is part of normal skin flora. Conversion from yeast form to the pathogenic mycelial form results in tinea versicolor, which is associated with the characteristic spaghetti and meatballs appearance on microscopy (ie, both hyphae and yeasts seen).





histopathology, not urine antigen testing.

**(Choice D)** *Cryptococcus neoformans* is a yeast with a thick, antiphagocytic, polysaccharide capsule that primarily causes infections in those who are immunocompromised (particularly patients with advanced AIDS). Although pulmonary infection can occur, disseminated disease is usually marked by meningoencephalitis (eg, headache, confusion, altered mental state).

**(Choice E)** *Malassezia* is a dimorphic fungus that is part of normal skin flora. Conversion from yeast form to the pathogenic mycelial form results in tinea versicolor, which is associated with the characteristic spaghetti and meatballs appearance on microscopy (ie, both hyphae and yeasts seen).

### Educational objective:

Tumor necrosis factor- $\alpha$  inhibitors are associated with impairments to the cell-mediated immune response and increase the risk of infection with intracellular bacteria and granulomatous fungi (eg, *Histoplasma capsulatum*). *Histoplasma* replicates within the intracellular space of macrophages and can spread from the lungs to the lymph nodes and the reticuloendothelial system (liver, spleen, bone marrow).

### References

- [The calcified lung nodule: what does it mean?](#)





A 7-year-old girl is brought to the office due to a diffuse rash. The father says she developed a lace-like, erythematous rash this morning on her stomach, back, and extremities. Two days ago, the girl developed red, flushed cheeks. She also had congestion, headache, and a low-grade fever for 3 days earlier this week. Last week, her younger brother had similar symptoms that resolved spontaneously. The infectious agent most likely responsible for this patient's disease replicates in progenitors of which of the following cell lines?

- ☐ A. Erythrocytes
- ☐ B. Hepatocytes
- ☐ C. Intestinal epithelial cells
- ☐ D. Lymphocytes
- ☐ E. Respiratory epithelial cells

**Submit**





A 7-year-old girl is brought to the office due to a **diffuse rash**. The father says she developed a lace-like, erythematous rash this morning on her stomach, back, and extremities. Two days ago, the girl developed red, **flushed cheeks**. She also had congestion, headache, and a low-grade fever for 3 days earlier this week. Last week, her younger brother had similar symptoms that resolved spontaneously. The infectious agent most likely responsible for this patient's disease replicates in progenitors of which of the following cell lines?

- ☒ A. Erythrocytes (57%)
- ☐ B. Hepatocytes (1%)
- ☐ C. Intestinal epithelial cells (2%)
- ☐ D. Lymphocytes (20%)
- ☐ E. Respiratory epithelial cells (17%)

Correct



57%

Answered correctly



43 secs

Time Spent



03/14/2021

Last Updated

Block Time Remaining: 00:09:50

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

## Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook



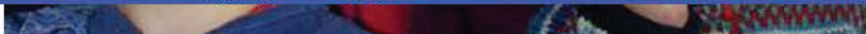
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End Block



**Erythema infectiosum**, or fifth disease, is a **benign** childhood illness caused by **parvovirus B19**, a single-stranded DNA virus. After a 1-2 week incubation period, a **nonspecific prodrome** (eg, malaise, congestion, headache, fever) is followed by an erythematous rash on the cheeks. This "**slapped-cheek**" rash, as shown in the image above, usually spares the nasolabial folds and develops after the initial symptoms have resolved. A **lacy, reticular rash** then follows, spreading over the trunk and extremities. The rash may result from immune complex deposition, the timing of which coincides with increasing levels of serum virus-specific IgM and IgG.

Parvovirus B19 replicates in **erythrocyte** precursors in the **bone marrow**. These cells express blood group P antigen (also known as globoside), which is the cellular receptor for parvovirus B19. Viral replication in the nucleus leads to cell lysis (ie, decreased reticulocytes and red blood cells). Acute and chronic sequelae of parvovirus B19 infection can occur in specific populations (eg, chronic anemia in immunosuppressed patients, aplastic crisis in those with underlying hematologic abnormalities such as sickle cell disease).

**(Choice B)** Hepatitis A-E viruses replicate within mature hepatocytes and cause inflammation and cell necrosis. Hepatitis B and C are chronic infections and the most common causes of cirrhosis and liver cancer.







Item 9 of 31

Question Id: 1495



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

### Exhibit Display



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

Block Time Remaining: 00:09:50

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Feedback



Suspend



End Block



cancer.

**(Choice C)** Rotavirus replicates in fully differentiated intestinal epithelial cells. The infected and damaged enterocytes slough into the intestinal lumen, leading to profuse watery diarrhea.

**(Choice D)** Mature lymphocytes are a common site of viral replication (eg, human herpesvirus-6 [HHV-6], HIV). HHV-6 causes roseola infantum, which presents as high fever followed by a diffuse maculopapular rash in children age <2.

**(Choice E)** Many common viruses (eg, influenza, parainfluenza, rhinovirus) replicate within respiratory epithelial cells (but not their precursors). Parainfluenza replication, for example, can be localized to only nasal and pharyngeal epithelium (eg, rhinorrhea, sore throat) or can spread more extensively, causing laryngotracheitis (croup), bronchiolitis, or pneumonia.

### Educational objective:

Erythema infectiosum (fifth disease) is caused by parvovirus B19 and presents with a nonspecific prodrome (eg, malaise, fever, congestion) followed by a classic "slapped-cheek" facial rash and a lacy, reticular body rash. Parvovirus is highly tropic for erythroid precursor cells and replicates predominantly in the bone marrow.

### References



A 64-year-old man comes to the office due to 2 days of dysuria, urinary frequency, and urgency. He recently underwent a cystoscopy for evaluation of hematuria. The patient has a history of hypertension, type 2 diabetes mellitus, and 30 pack-years of cigarette smoking. His temperature is 38.2 C (100.8 F). On examination, there is suprapubic tenderness on deep palpation but no costovertebral angle tenderness. Urinalysis findings are as follows:

Leukocyte esterase	positive
Nitrites	negative
Bacteria	many
White blood cells	20-30/hpf
Red blood cells	many/hpf

Midstream urine culture grows gram-positive cocci in chains with growth >100,000 colony-forming units/mL. The organism responsible for this patient's condition is most likely to demonstrate which of the following?





Bacteria

many

White blood cells

20-30/hpf

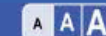
Red blood cells

many/hpf

Midstream urine culture grows gram-positive cocci in chains with growth >100,000 colony-forming units/mL. The organism responsible for this patient's condition is most likely to demonstrate which of the following?

- ☐ A. Ability to decompose hydrogen peroxide
- ☐ B. Gamma hemolysis on blood agar
- ☐ C. Growth only in absence of oxygen
- ☐ D. Possession of cytochrome oxidase
- ☐ E. Production of golden yellow pigments

**Submit**



Bacteria

many

White blood cells

20-30/hpf

Red blood cells

many/hpf

Midstream urine culture grows **gram-positive cocci** in chains with growth >100,000 colony-forming units/mL. The organism responsible for this patient's condition is most likely to demonstrate which of the following?

- ☐ A. Ability to decompose hydrogen peroxide (20%)
- ☒ B. Gamma hemolysis on blood agar (55%)
- ☐ C. Growth only in absence of oxygen (4%)
- ☐ D. Possession of cytochrome oxidase (8%)
- ☐ E. Production of golden yellow pigments (11%)

Correct

55%



01 min, 10 secs



12/03/2020

Block Time Remaining: 00:11:00

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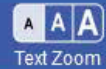
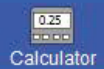
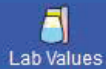
Feedback



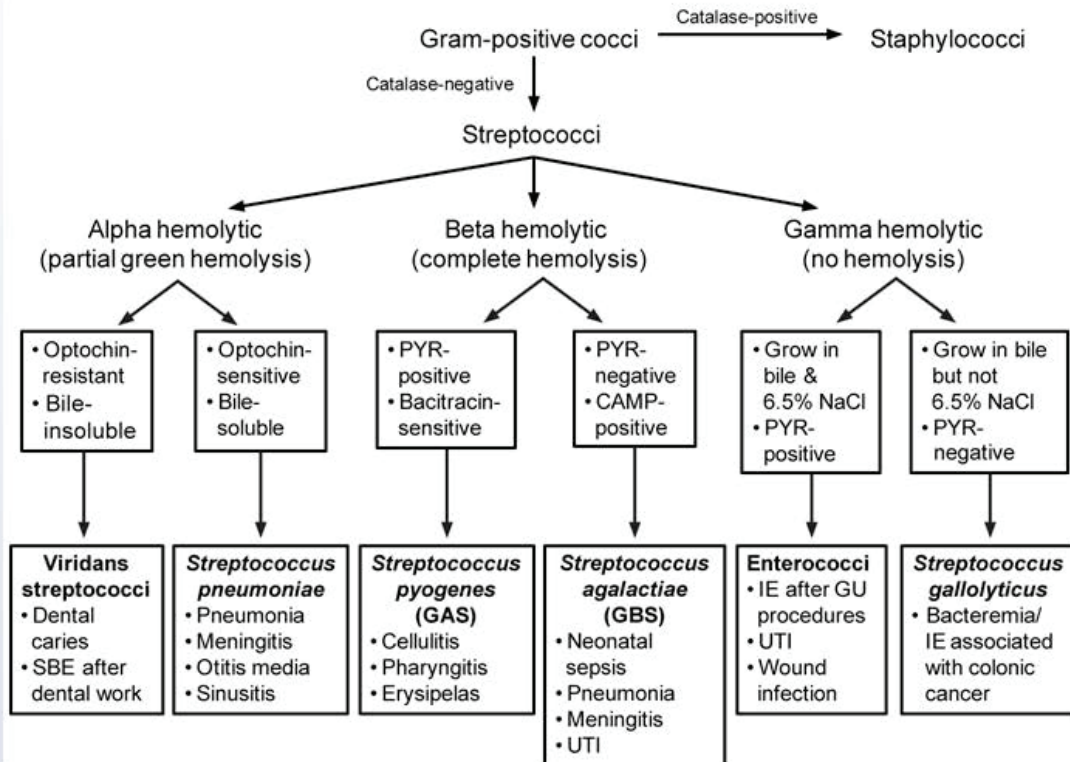
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End Block



## Microbiological laboratory identification of streptococci





This patient who recently underwent a genitourinary procedure (cystoscopy) has a urinary tract infection caused by **Enterococcus**. This organism has a morphology of **gram-positive cocci** in pairs and chains and, when grown on blood agar, reveals no hemolysis (**gamma hemolysis**). Other characteristics of enterococci include pyrrolidonyl arylamidase (PYR) positivity and ability to grow in bile and in 6.5% sodium chloride. They are unable to convert nitrates to nitrites, explaining this patient's negative result on urinalysis nitrite.

Enterococci are part of the normal intestinal flora of humans and animals. *Enterococcus faecalis* and *E faecium* are the most prevalent species cultured from humans and can cause urinary tract infection, bacteremia/endocarditis, wound infection, or intraabdominal or pelvic infection in the nosocomial setting. Enterococci have both intrinsic (beta-lactams, macrolides, aminoglycosides, trimethoprim-sulfamethoxazole) and acquired (vancomycin) resistance to antibiotics, making them important nosocomial pathogens.

**(Choice A)** The ability to decompose hydrogen peroxide is suggestive of the presence of catalase, which would indicate *Staphylococcus* (which are gram-positive cocci in clusters not chains).

**(Choice C)** Enterococci are aerobic organisms. Examples of anaerobic gram-positive cocci include *Pentostreptococcus* and *Micrococcus*.

would indicate *Staphylococcus* (which are gram-positive cocci in clusters not chains).

**(Choice C)** Enterococci are aerobic organisms. Examples of anaerobic gram-positive cocci include *Peptostreptococcus* and *Micrococcus*.

**(Choice D)** Oxidase positivity (possession of cytochrome oxidase) can help identify certain gram-negative organisms (eg, *Pseudomonas*).

**(Choice E)** *Staphylococcus aureus* produces golden yellow pigments. Other bacteria producing pigments include *Pseudomonas aeruginosa* (blue-green) and *Serratia marcescens* (red).

### Educational objective:

*Enterococcus* is an important cause of urinary tract infections. These organisms are gram-positive cocci in pairs and chains and, when grown on blood agar, they do not cause hemolysis (gamma-hemolytic).

### References

- Emergence of *Enterococcus* as a significant pathogen.
- The life and times of the *Enterococcus*.

Microbiology

Microbiology (General Principles)

Urinary tract infection

Subject

System

Topic

Block Time Remaining: 00:11:00

TUTOR

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1



Feedback



Suspend



End Block



A 4-year-old boy is brought to the physician by his mother with decreased appetite, abdominal cramps, and diarrhea over the last 3 days. The stools were initially watery but have now become bloody. On physical examination, his temperature is 100.4 F (38 C). There are signs of dehydration and he has a mildly distended abdomen with diffuse pain elicited on palpation. Stool studies are positive for fecal leukocytes and occult blood. Fecal cultures grow non-lactose fermenting, gram-negative rods on MacConkey agar. The bacteria ferment glucose without gas production, do not generate hydrogen sulfide when grown on triple sugar iron agar, and cannot replicate at refrigeration temperatures. Which of the following bacterial factors is the most important during the pathogenesis of this patient's disease?

- ☐ A. Exotoxin production
- ☐ B. Intestinal colonization
- ☐ C. Mucosal invasion
- ☐ D. Proliferation in lymph nodes
- ☐ E. Survival in the circulation







diarrhea over the last 3 days. The stools were initially watery but have now become bloody. On physical examination, his temperature is 100.4 F (38 C). There are signs of dehydration and he has a mildly distended abdomen with diffuse pain elicited on palpation. Stool studies are positive for fecal leukocytes and occult blood. Fecal cultures grow non-lactose fermenting, gram-negative rods on MacConkey agar. The bacteria ferment glucose without gas production, do not generate hydrogen sulfide when grown on triple sugar iron agar, and cannot replicate at refrigeration temperatures. Which of the following bacterial factors is the most important during the pathogenesis of this patient's disease?

- ☐ A. Exotoxin production (31%)
- ☐ B. Intestinal colonization (8%)
- ☒ C. Mucosal invasion (55%)
- ☐ D. Proliferation in lymph nodes (2%)
- ☐ E. Survival in the circulation (1%)

Correct

55%



02 mins, 10 secs



03/24/2021

Block Time Remaining: 00:13:10

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Feedback



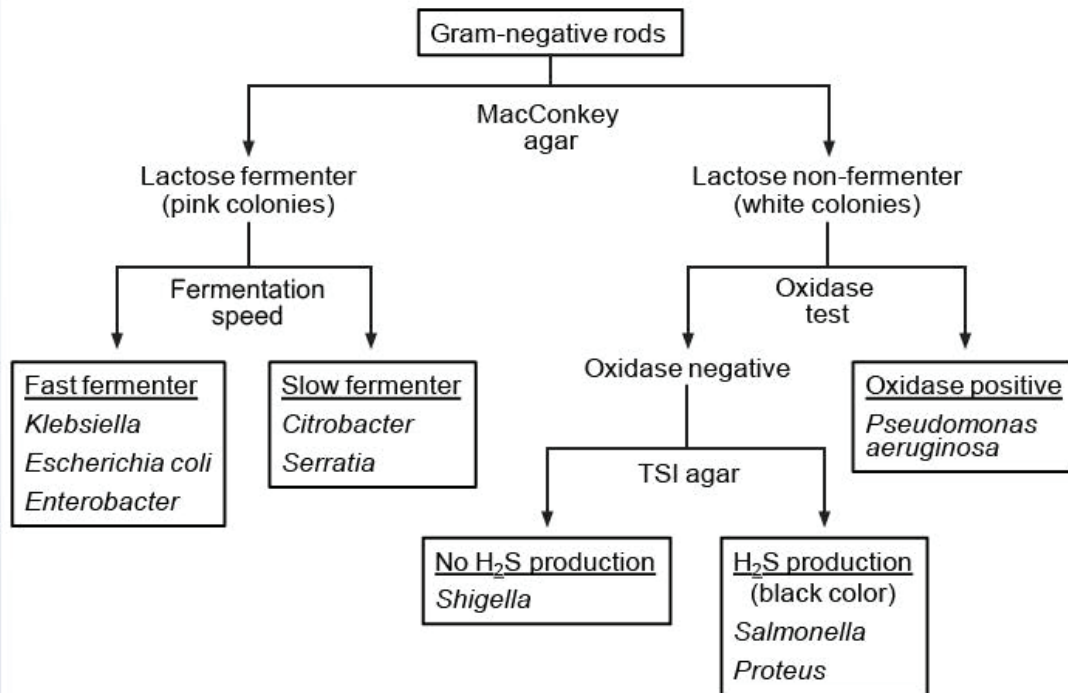
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End Block



## Characteristics of gram-negative bacteria



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This patient's fever, abdominal cramps, and bloody diarrhea (**dysentery**) are consistent with bacterial enteritis. His stool culture results are most specific for a *Shigella* species (*Shigella sonnei* being most common in the United States). **Shigella** is transmitted via the fecal-oral route and is never a component of the normal bacterial gut flora. Shigellosis is primarily a pediatric disease but also shows a predilection for men who have sex with men and adults in skilled nursing facilities. *Shigella* species are non-lactose fermenting organisms that produce acid (not gas) during glucose fermentation (in contrast to *Escherichia coli*). Furthermore, *Shigella* species are non-motile and do not produce H<sub>2</sub>S (in contrast to *Salmonella*).

**Mucosal invasion** is the essential pathogenic mechanism for *Shigella* infection. *Shigella* invades the gastrointestinal mucosa, particularly via the M cells that overlie Peyer's patches. After cell entry, *Shigella* is able to lyse its containment vacuole and enter the cytosolic compartment. It then can induce apoptosis of the host cell and spread to adjacent cells via protrusions created through host-cell **actin polymerization**. *Shigella* invasion triggers a robust host inflammatory response that is largely mediated by neutrophils.

**(Choice A)** Some strains of *Shigella* produce shiga toxin, which damages the intestinal mucosa by inactivating the 60S ribosomal subunit, halting cellular protein synthesis. However, shiga toxin plays a minor, nonessential role in the disease process, as nontoxigenic strains also cause shigellosis.







**(Choice B)** Intestinal colonization with *Shigella* does not occur as the bacterium is highly pathogenic; transmission of as few as 10-100 organisms is sufficient to cause disease. If *Shigella* is isolated from a stool culture, an active infection is taking place.

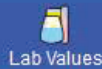
**(Choice D)** Proliferation in lymph nodes is not a characteristic of *Shigella*. In contrast, both *Salmonella typhi* and *Yersinia enterocolitica* (grows at low temperatures like *Listeria*) can gain access to the lymphatics and proliferate in the mesenteric lymph nodes. *Y enterocolitica* can cause inflammation and enlargement of the lymphoid tissue around the appendix and terminal ileum ("pseudoappendicitis"), leading to right lower quadrant pain that can be confused with acute appendicitis.

**(Choice E)** *Shigella* infections rarely cause bacteremia, as the bacterium is readily phagocytosed and destroyed after entering the bloodstream. Enteric bacteremia is more likely to be caused by *E coli*, *S typhi* (typhoid fever), *Klebsiella*, and *Proteus*.

### Educational objective:

*Shigella* is a non-motile, non-lactose fermenting organism that does not produce  $H_2S$  when grown on triple sugar iron agar. Mucosal invasion of the M cells that overlie Peyer's patches is an essential pathogenic mechanism for *Shigella* infection. *Shigella* then escapes the phagosome and spreads laterally to other epithelial cells via actin polymerization.





A 6-year-old previously healthy girl is brought to the office due to diarrhea and abdominal pain. She started having watery diarrhea after a barbeque dinner 4 days ago; her stools became grossly bloody 2 days later. Her mother also had similar symptoms. The patient's temperature is 37 C (98.7 F). The abdomen is soft with mild generalized tenderness. Stool culture is performed on sorbitol-MacConkey agar and reveals sorbitol-negative colonies with biochemical properties of *Escherichia coli*. Enzyme immunoassay detects a substance capable of inhibiting protein synthesis in human cells. The substance detected in this patient is most similar to the toxin produced by which of the following bacteria?

- ☐ A. *Clostridium difficile*
- ☐ B. *Proteus mirabilis*
- ☐ C. *Pseudomonas aeruginosa*
- ☐ D. *Salmonella typhi*
- ☐ E. *Shigella dysenteriae*
- ☐ F. *Vibrio cholerae*





having watery diarrhea after a barbeque dinner 4 days ago; her stools became grossly bloody 2 days later. Her mother also had similar symptoms. The patient's temperature is 37 C (98.7 F). The abdomen is soft with mild generalized tenderness. Stool culture is performed on sorbitol-MacConkey agar and reveals sorbitol-negative colonies with biochemical properties of *Escherichia coli*. Enzyme immunoassay detects a substance capable of inhibiting protein synthesis in human cells. The substance detected in this patient is most similar to the toxin produced by which of the following bacteria?

- ☐ A. *Clostridium difficile* (2%)
- ☐ B. *Proteus mirabilis* (0%)
- ☒ C. *Pseudomonas aeruginosa* (6%)
- ☐ D. *Salmonella typhi* (2%)
- ☒ E. *Shigella dysenteriae* (85%)
- ☐ F. *Vibrio cholerae* (2%)

**Incorrect**

Correct answer



85%

Answered correctly



22 secs

Time spent



12/20/2020

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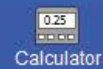
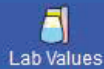


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### Mechanism of action of selected bacterial exotoxins

Organism	Toxin	Mechanism & effects
<i>Bacillus anthracis</i>	Anthrax exotoxin	Edema factor: Increases cyclic AMP concentration by acting as an adenylate cyclase, causing edema & phagocyte dysfunction
		Lethal factor: Zinc-dependent protease that inhibits mitogen-activated protein kinase signaling, causing apoptosis & multisystem physiologic disruption
<i>Bordetella pertussis</i>	Pertussis toxin	Disinhibits adenylate cyclase through G <sub>i</sub> ADP-ribosylation, increasing cAMP levels; causes edema & phagocyte dysfunction
	Adenylate cyclase toxin	Functions as an adenylate cyclase, increasing cAMP levels; causes edema & phagocyte dysfunction
<i>Clostridium botulinum</i>	Botulinum toxin	Blocks presynaptic release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis



<i>Clostridium difficile</i>	Toxin A	Recruits & activates neutrophils, leading to release of cytokines that cause mucosal inflammation, fluid loss & diarrhea
	Toxin B	Induces actin depolymerization, leading to mucosal cell death, bowel wall necrosis & pseudomembrane formation
<i>Shigella dysenteriae</i>	Shiga toxin	Halts protein synthesis by disabling the 60S ribosomal subunit, leading to intestinal epithelial cell death & diarrhea
<i>Streptococcus pyogenes</i>	Pyrogenic exotoxin	Acts as a superantigen, inducing fever & shock; associated with scarlet fever & streptococcal toxic shock syndrome
	Streptolysin O&S	Damages erythrocyte membranes, causing beta hemolysis

**Shiga-like toxins** (Stx) (Vero cytotoxins [VT]) are produced by **enterohemorrhagic *Escherichia coli***.

Stx-I (VT1) can inhibit **protein synthesis** in human cells and is closely related to the Shiga toxin produced by *Shigella dysenteriae*. It is an AB toxin (active A subunit and 5 binding B subunits). The plasmid coding for it is transmitted by a temperate bacteriophage. The B subunits, which form pentamers with a central pore, recognize specific receptors on target cells and induce receptor-mediated endocytosis and toxin



pore, recognize specific receptors on target cells and induce receptor-mediated endocytosis and toxin internalization. Subsequently, the enzymatically active A subunit is released and catalyses the removal of a specific adenine residue, thereby preventing tRNA binding to the 60S ribosomal subunit and inhibiting protein synthesis. This leads to intestinal mucosal cell death and direct toxicity to renal epithelial cells.

**(Choice A)** *Clostridium difficile* produces toxin A (enterotoxin) and toxin B (cytotoxin) and causes pseudomembranous colitis, most commonly in patients recently treated with antibiotics. Toxin B depolymerizes actin filaments, causing gastrointestinal mucosal cell death.

**(Choice B)** *Proteus mirabilis* does not produce toxins.

**(Choice C)** *Pseudomonas aeruginosa* produces exotoxin A, similar in function to diphtheria toxin in that it halts human cellular protein synthesis by inhibiting elongation factor-2. The growing protein chain is unable to change positions in the ribosome to allow binding of a new tRNA, resulting in translation arrest.

**(Choice D)** *Salmonella typhi* (cause of typhoid fever) enters the human digestive tract orally, penetrates the intestinal mucosa, and travels to mesenteric lymph nodes, where it multiplies and is phagocytosed by macrophages within which it can survive. Typhoid fever is characterized by fever, abdominal pain, diarrhea and/or constipation, and faintly erythematous macules on the abdomen ("rose spots").

**(Choice E)** *Vibrio cholerae*, the causative agent of cholera, produces the enterotoxin cholera toxin, which







**(Choice D)** *Salmonella typhi* (cause of typhoid fever) enters the human digestive tract orally, penetrates the intestinal mucosa, and travels to mesenteric lymph nodes, where it multiplies and is phagocytosed by macrophages within which it can survive. Typhoid fever is characterized by fever, abdominal pain, diarrhea and/or constipation, and faintly erythematous macules on the abdomen ("rose spots").

**(Choice F)** *Vibrio cholerae*, the causative agent of cholera, produces the enterotoxin cholera toxin, which acts similarly to the heat-labile toxin of enterotoxigenic *Escherichia coli*. It increases intracellular cAMP in intestinal mucosal cells, leading to decreased absorption and increased secretion of sodium, chloride, and water.

### Educational objective:

Shiga-like toxins (Vero cytotoxins), produced by enterohemorrhagic *Escherichia coli*, are nearly identical to the Shiga toxin produced by *Shigella dysenteriae*. They inhibit the 60S ribosomal subunit in human cells, thereby blocking protein synthesis by preventing binding of tRNA.

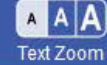
Microbiology  
Subject

Microbiology (General Principles)  
System

Acute diarrhea  
Topic

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A 23-year-old woman participates in a research study evaluating the effect of monoclonal antibodies on viral infection. The patient has no past medical history and takes no medications. She has not been ill recently. During the study, a peripheral blood specimen is obtained. CD19 positive cells are isolated, purified, and exposed to monoclonal antibodies against cell surface complement receptor CD21. The cells are subsequently incubated along with several viruses being studied. Initial exposure to monoclonal antibodies against CD21 is most likely to prevent cell infection with which of the following viruses?

- ☐ A. Adenovirus
- ☐ B. Cytomegalovirus
- ☐ C. Epstein-Barr virus
- ☐ D. Human immunodeficiency virus
- ☐ E. Parvovirus B19

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Previous



Next



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A 23-year-old woman participates in a research study evaluating the effect of monoclonal antibodies on viral infection. The patient has no past medical history and takes no medications. She has not been ill recently. During the study, a peripheral blood specimen is obtained. CD19 positive cells are isolated, purified, and exposed to monoclonal antibodies against cell surface complement receptor CD21. The cells are subsequently incubated along with several viruses being studied. Initial exposure to monoclonal antibodies against CD21 is most likely to prevent cell infection with which of the following viruses?

- ☐ A. Adenovirus (1%)
- ☐ B. Cytomegalovirus (4%)
- ☒ C. Epstein-Barr virus (84%)
- ☐ D. Human immunodeficiency virus (5%)
- ☐ E. Parvovirus B19 (4%)

Correct

 84%  
Answered correctly 14 secs  
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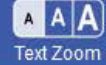


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The initial attachment of the virion envelope or capsid surface proteins to the complementary host cell surface receptors is essential to viral tropism for specific tissues and invasion of cells. Many viruses bind to normal host cell plasma membrane receptors to enter host cells.

**Epstein-Barr virus** (EBV) is a herpesvirus responsible for acute infectious mononucleosis, nasopharyngeal carcinoma, and certain lymphomas (eg, Burkitt lymphoma). More than 90% of the normal adult population is seropositive for EBV, which is primarily transmitted through contact with oropharyngeal secretions. The EBV envelope glycoprotein gp350 binds to **CD21** (also known as CR2), the cellular receptor for the C3d complement component. CD21 is normally present on the surface of **B cells** (CD19-positive cells) and nasopharyngeal epithelial cells. Therefore, exposure to a monoclonal anti-CD21 antibody could interfere with EBV attachment to B cells.

**(Choice A)** Adenovirus has hexon and penton capsomeres on its surface. Rodlike structures ("fibers") that project from the penton base capsomeres are responsible for mediating adsorption to host cells. The cell receptor for most adenovirus fibers is a transmembrane protein member of the immunoglobulin superfamily.

**(Choice B)** Like other herpesviruses, cytomegalovirus requires initial contact with glycosaminoglycan chains on host cell surface proteoglycans for entry into the host cell. It does not require contact with CD21.





**(Choice D)** HIV viruses attach to their major target host cells (CD4<sup>+</sup> T cells) primarily via the binding of viral envelope glycoprotein gp120 to the cellular CD4 transmembrane glycoprotein and the coreceptor (CCR5 or CXCR4). The HIV envelope then undergoes a conformational change that activates gp41 and initiates membrane fusion.

**(Choice E)** Parvovirus B19 is thought to attach to human erythroid cells via the blood group P antigen (globoside), which is expressed by mature erythrocytes, erythroid progenitors, megakaryocytes, placenta, and the fetal liver and heart. Immature cells of the erythroid family (eg, adult bone marrow, fetal liver) are most vulnerable to parvovirus B19 infection.

### Educational objective:

The initial attachment of the virion envelope or capsid surface proteins to the complementary host cell surface receptors is essential to viral tropism for specific tissues and invasion of cells. Many viruses bind to normal host cell plasma membrane receptors to enter host cells. Known host cell receptor and virion/virion protein binding specificities include: CD4 with HIV gp120, CD21 with Epstein-Barr virus gp350, and erythrocyte P antigen with parvovirus B19.





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

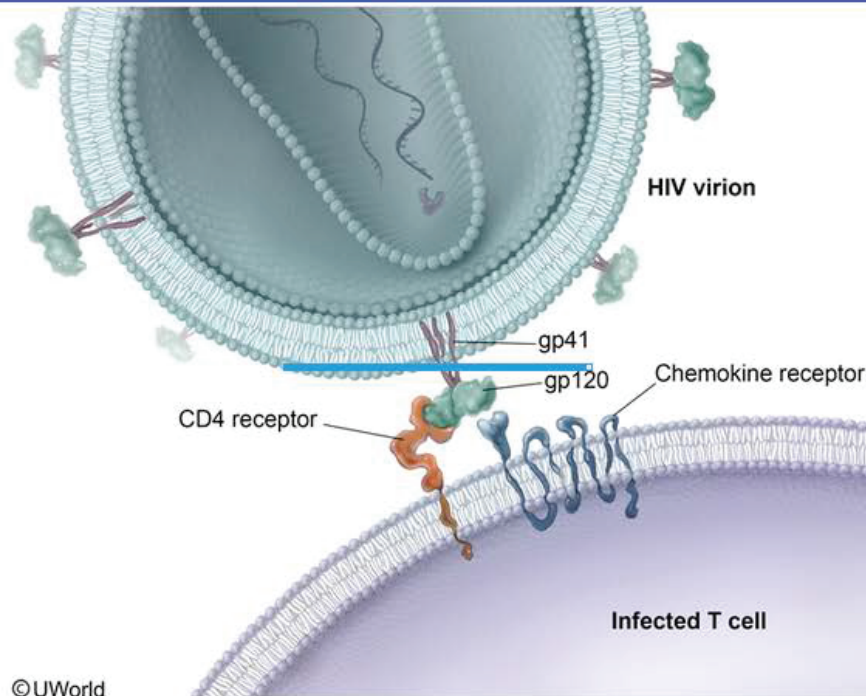
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Mark



Previous



Next



Full Screen



Tutorial



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Notes



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A virologist is researching acyclovir-resistant herpes simplex virus (HSV). Viral DNA analysis reveals a mutation in the thymidine kinase gene, resulting in a mutated enzyme that does not phosphorylate acyclovir to its active form. In an experiment, a resistant HSV type 2 strain containing this mutation is cultured in a cell line, and the cell culture is coinfectd with a nonresistant HSV type 1 strain. It is found that some of the newly produced type 1 virions acquire resistance to acyclovir, and subsequent progeny continue to be resistant. Which of the following mechanisms best explains the observed findings?

- ☐ A. Interference
- ☐ B. Phenotypic mixing
- ☐ C. Reassortment
- ☐ D. Recombination
- ☐ E. Transformation

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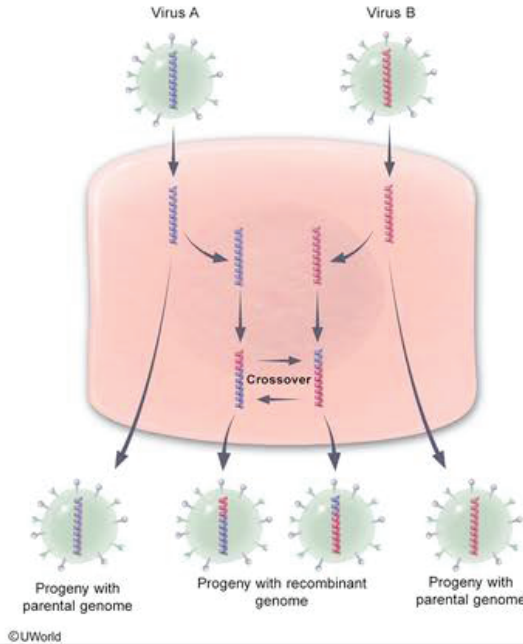
- ☐ A. Interference (0%)
- ☐ B. Phenotypic mixing (9%)
- ☐ C. Reassortment (21%)
- ☒ D. Recombination (40%)
- ☐ E. Transformation (28%)

Correct

 40%  
Answered correctly 01 min, 55 secs  
Time Spent 02/23/2021  
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### Exhibit Display

#### Recombination



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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This scenario describes the exchange of genetic information between 2 virus strains that have **nonsegmented, double-stranded** DNA genomes. **Recombination** refers to the exchange of genes between 2 chromosomes via **crossing over** within homologous regions. The resulting progeny can have recombined genomes with traits from both parent viruses. In this case, the thymidine kinase genes in HSV type 1 and 2 virions are likely to have significant sequence similarity, allowing cross over to occur with relatively high frequency.

**(Choice A)** Interference occurs when one virus inhibits replication and/or release of a second virus that is infecting the same cell. Simple interference would not result in recombinant progeny virions.

**(Choice B)** **Phenotypic mixing** can occur when a host cell is coinfecting with 2 viral strains and progeny virions contain parental genome from one strain and nucleocapsid (or envelope) proteins from the other strain. This may result in progeny acquiring additional traits (eg, enhanced ability to infect new host cells due to different nucleocapsid proteins). However, as the genome is unchanged, subsequent progeny would not retain these traits.

**(Choice C)** **Reassortment** refers to changes in genomic composition that occur when host cells are coinfecting with 2 **segmented** viruses that exchange whole genome segments. This process can cause



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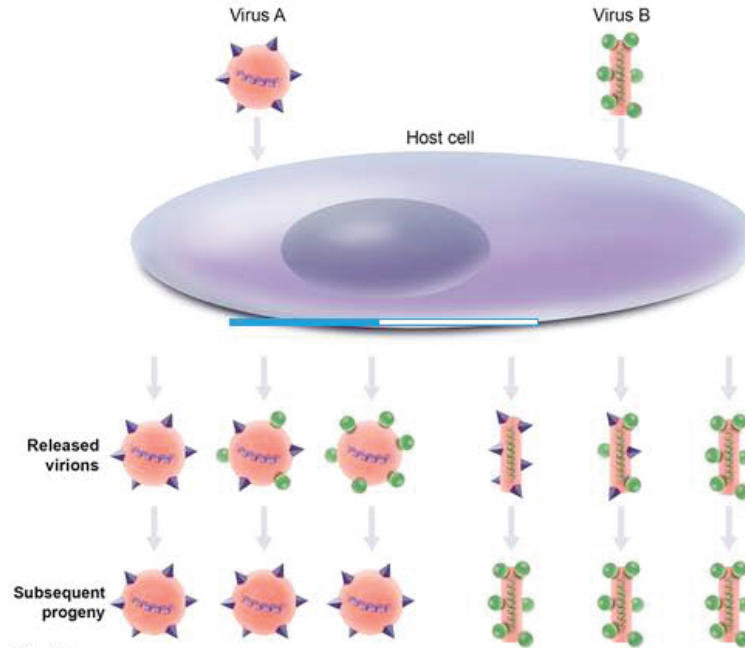


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### Exhibit Display Phenotypic mixing



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

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strain. This may result in progeny acquiring additional traits (eg, enhanced ability to infect new host cells due to different nucleocapsid proteins). However, as the genome is unchanged, subsequent progeny would not retain these traits.

**(Choice C)** **Reassortment** refers to changes in genomic composition that occur when host cells are coinfecting with 2 **segmented** viruses that exchange whole genome segments. This process can cause sudden alterations in surface antigens of the viral progeny, as observed with the highly mutagenic influenza virus. However, because the herpesvirus genome is nonsegmented, it does not engage in reassortment.

**(Choice E)** Transformation is the uptake of naked DNA by a prokaryotic or eukaryotic cell. In virology, transformation also describes incorporation of viral DNA into a host cell chromosome (lysogeny). Transformation alters the genetic composition of the host cell but typically causes no genomic change in progeny virions.

### Educational objective:

Recombination refers to gene exchange that occurs through the crossing over of 2 double-stranded DNA molecules. Reassortment describes the mixing of genome segments in segmented viruses that infect the same host cell.

Microbiology

Microbiology (General Principles)

Viral genetics

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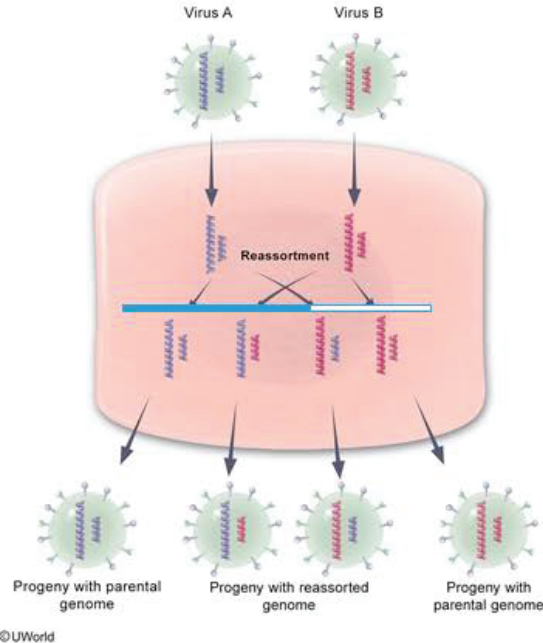


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## Exhibit Display

## Reassortment (segmented viruses)



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A 23-year-old woman comes to the emergency department due to 4 days of intermittent fever, chills, and diaphoresis accompanied by fatigue, myalgia, and dull headache. She recently returned from a 3-month trip to India, where she worked for a nongovernmental organization. The patient had similar symptoms during her first month abroad that improved after several days of treatment. She has no other medical history and takes no medications. Temperature is 38.3 C (101 F), blood pressure is 110/70 mm Hg, and pulse is 100/min. Physical examination shows mild jaundice and hepatosplenomegaly. Laboratory results reveal anemia and elevated indirect bilirubin levels. A peripheral blood smear using Giemsa stain shows intraerythrocytic ringed inclusions. This patient's current symptoms are most likely due to reactivation of a dormant infection in which of the following?

- ☐ A. Gall bladder
- ☐ B. Liver
- ☐ C. Lung
- ☐ D. Lymph nodes
- ☐ E. Red blood cells



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- ☐ A. Gall bladder
- ☐ B. Liver
- ☐ C. Lung
- ☐ D. Lymph nodes
- ☐ E. Red blood cells
- ☐ F. Spleen

Submit







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- ☐ A. Gall bladder (1%)
- ☒ B. Liver (87%)
- ☐ C. Lung (0%)
- ☐ D. Lymph nodes (0%)
- ☐ E. Red blood cells (7%)
- ☐ F. Spleen (2%)

Correct

87%



01 min, 15 secs



10/07/2020

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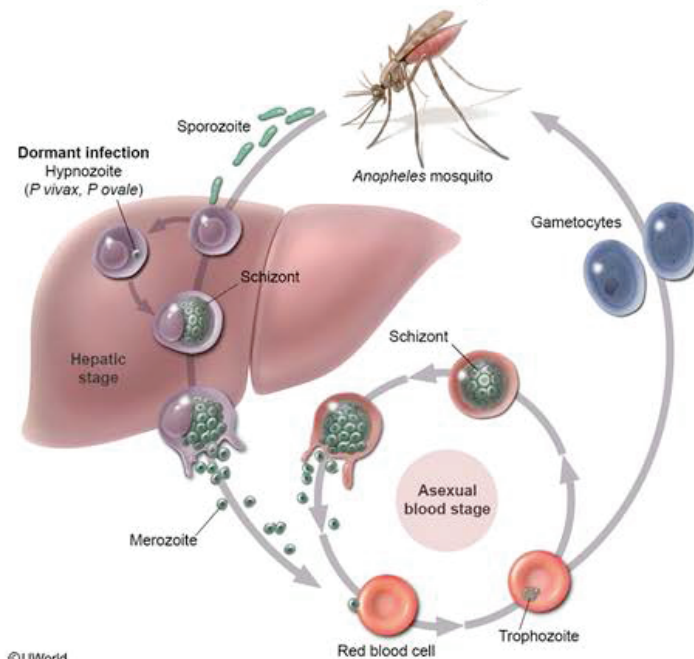
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## Exhibit Display

## Malaria life cycle



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Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

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**Malaria** is a mosquito-borne, protozoal infection caused by *Plasmodium* species. Transmission occurs when an infected female *Anopheles* mosquito injects *Plasmodium* sporozoites into subcutaneous capillaries during feeding. Within hours, sporozoites attach to and enter hepatocytes and undergo asexual reproduction. This results in the production of tens of thousands of daughter cells (merozoites) that eventually rupture the hepatocyte and spread to erythrocytes, where another asexual reproduction cycle occurs.

Manifestations of malaria arise due to erythrocyte rupture and include fever, flu-like symptoms (eg, myalgia, fatigue, headache, chills), anemia, and indirect bilirubinemia (hepatosplenomegaly is also common). The diagnosis is confirmed when **trophozoites** (intraerythrocytic, ringed inclusions) are seen on peripheral blood smear using Giemsa stain.

Although many different *Plasmodium* species cause malaria, the 2 dominant organisms are *P falciparum* (in Africa) and ***P vivax*** (in non-African countries). This patient who traveled to India was likely infected with *P vivax*. Unlike *P falciparum*, *P vivax* (and *P ovale*) sporozoites can undergo a **dormant hepatic phase** (hypnozoite stage) that may cause **recurrent parasitemia** and symptoms weeks or months after initial infection. Individuals with these strains of malaria must be treated with a combination of drugs that target both the erythrocyte phase (eg, chloroquine) and the dormant hepatic phase (ie, **primaquine**) to ensure clearance. Patients who are treated with a medication that only targets the erythrocyte phase (as was







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

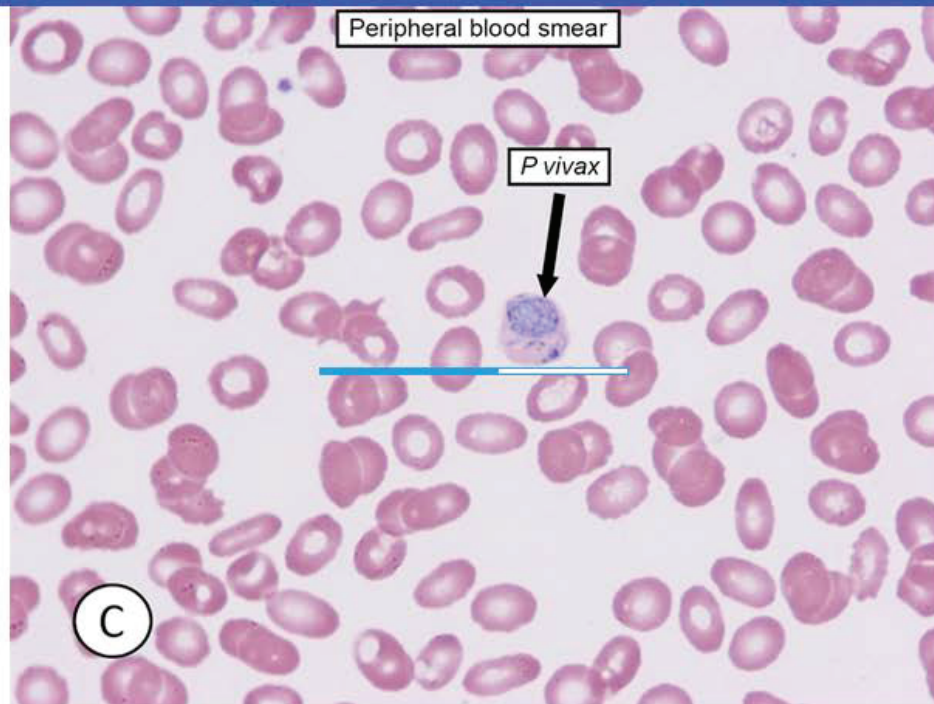
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Malaria is a mosquito borne, protozoal infection caused by *Plasmodium* species. Transmission occurs

## Exhibit Display



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clearance. Patients who are treated with a medication that only targets the erythrocyte phase (as was

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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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clearance. Patients who are treated with a medication that only targets the erythrocyte phase (as was likely in this case) may initially improve but are likely to develop recurrent symptoms when the dormant hepatic hypnozoites reactivate.

**(Choice A)** *Salmonella typhi* can spread from the gastrointestinal tract to the gallbladder, which can lead to long-term gallbladder colonization. Typhoid fever is usually associated with a week of stepwise fever followed by a week of "rose spots" and abdominal pain and then possible complications such as abdominal bleeding/perforation and hepatosplenomegaly.

**(Choice C)** Tuberculosis most commonly reactivates from granulomas in the lung, but reactivation can also arise from latent foci in the liver, spleen, or kidneys (~15% of cases). Tuberculosis reactivation usually causes fever, weight loss, and pulmonary manifestations (eg, cough, dyspnea, cavitary disease).

**(Choice D)** Numerous infections can reactivate from the lymph nodes, including HIV, Epstein-Barr virus, and tuberculosis. These infections are not associated with intraerythrocytic, ringed organisms.

**(Choice E)** Malaria infects and lyses erythrocytes. However, dormant infection occurs in the liver.

### Educational objective:

*Plasmodium vivax* is the most common cause of malaria in non-African countries. It is transmitted by the female *Anopheles* mosquito and is associated with a latent liver phase that must be treated (with



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long-term gallbladder colonization. Typhoid fever is usually associated with a week of stepwise fever followed by a week of "rose spots" and abdominal pain and then possible complications such as abdominal bleeding/perforation and hepatosplenomegaly.

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**(Choice E)** Malaria infects and lyses erythrocytes. However, dormant infection occurs in the liver.

### Educational objective:

*Plasmodium vivax* is the most common cause of malaria in non-African countries. It is transmitted by the female *Anopheles* mosquito and is associated with a latent liver phase that must be treated (with primaquine) independently of the erythrocytic phase to fully eliminate the organism.

### References

- [Malaria.](#)





A 24-year-old female presents to your office with burning urination, urgency and frequency. She is sexually active. Urine cultures show catalase-positive, gram-positive cocci. The organism responsible for this patient's symptoms is most likely to be:

- ☐ A. Coagulase positive
- ☐ B. Hemolytic
- ☐ C. Novobiocin resistant
- ☐ D. DNase positive
- ☐ E. Yellow pigment producer

**Submit**



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Previous



Next



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Lab Values



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Settings

A 24-year-old female presents to your office with burning urination, urgency and frequency. She is sexually active. Urine cultures show catalase-positive, gram-positive cocci. The organism responsible for this patient's symptoms is most likely to be:

- ☐ A. Coagulase positive (15%)
- ☐ B. Hemolytic (6%)
- ☒ C. Novobiocin resistant (72%)
- ☐ D. DNase positive (2%)
- ☐ E. Yellow pigment producer (4%)

**Correct** 72%  
Answered correctly 37 secs  
Time Spent 01/30/2021  
Last Updated

Explanation

Block Time Remaining: 00:17:36

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<https://t.me/USMLEWorldStep1>

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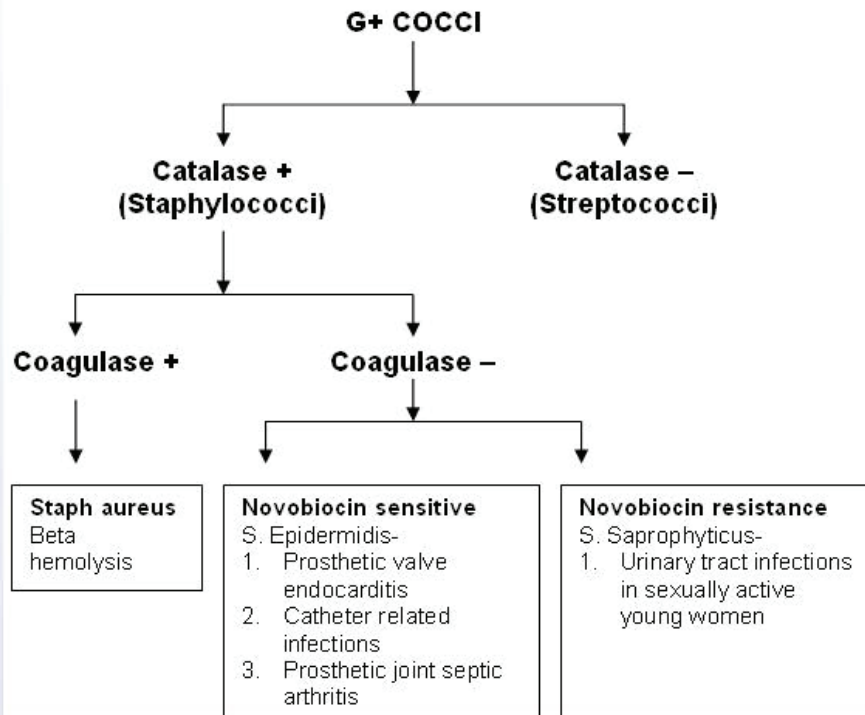
Feedback



Suspend



End Block



The Staphylococci are Gram-positive cocci that form clusters, pairs and, rarely, short chains. The catalase test (with 3% hydrogen peroxide) differentiates Streptococci (catalase-negative) from Staphylococci





Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The Staphylococci are Gram-positive cocci that form clusters, pairs and, rarely, short chains. The catalase test (with 3% hydrogen peroxide) differentiates Streptococci (catalase-negative) from Staphylococci (catalase-positive). The ability to clot blood plasma (slide and tube coagulase tests) separates Staphylococci into two groups: the coagulase-positive Staphylococci, which constitutes the most pathogenic species *Staphylococcus aureus*, and coagulase-negative staphylococci (CNS), which constitutes *S. epidermidis*, *S. Saprophyticus*, *S. haemolyticus*, and 30+ other species. The coagulase-negative staphylococci exist as part of the normal flora on the skin and in the throat and nose, and only some species can cause infections.

*S. saprophyticus* is a common cause of urinary tract infection; it is responsible for almost half of all UTIs in sexually active young women. *S. saprophyticus* is resistant to novobiocin. When catalase-positive, coagulase-negative gram-positive cocci in clusters are isolated from urine specimens of the above group of patients, the laboratory performs a novobiocin test to distinguish this organism from other similar pathogens.

**(Choice A)** Coagulase positivity is a characteristic of *S. aureus*; this is how *S. aureus* is differentiated from the other species of Staphylococci that do not express coagulase.

**(Choice B)** Hemolysis is a typical feature of Streptococci (streptolysin O and streptolysin S) and





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Coagulase positivity is a characteristic of *S. aureus*; this is how *S. aureus* is differentiated from the other species of Staphylococci that do not express coagulase.

**(Choice B)** Hemolysis is a typical feature of Streptococci (streptolysin O and streptolysin S) and *Staphylococcus aureus* (hemolysin). *S. saprophyticus* does not cause hemolysis.

**(Choice D)** DNase is produced by group A *streptococcus*. DNase degrades DNA in pus to facilitate spread of the organism. Anti DNase can be used as a laboratory test in patients who have had streptococcal infection followed by glomerulonephritis. DNase is not produced by *S. saprophyticus*.

**(Choice E)** Yellow pigment is produced by *Staphylococcus aureus*. *Staphylococcus aureus* usually does not cause urinary tract infections. If *S. aureus* is cultured from the urine you should suspect a metastatic infection from another location in the body (an abscess or infective endocarditis etc.)

### Educational Objective:

*S saprophyticus* is responsible for almost half of all UTIs in sexually active young women. *Staphylococcus saprophyticus* belongs to coagulase negative staphylococci and is unique among these because it is resistant to novobiocin.

Microbiology

Microbiology (General Principles)

Urinary tract infection

Block Time Remaining: 00:17:36

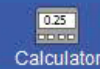
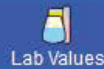
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Feedback

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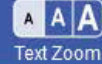
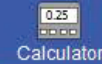
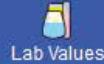
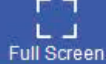
An epidemiologic study is conducted after a sudden increase in the rate of severe postoperative infections in a rural hospital. It is determined that all the patients who developed the infection were operated on with surgical instruments sterilized by a specific autoclave machine. The machine was found to be inadequately sterilizing the equipment due to a malfunction limiting the temperature to 100 C (212 F) during the 15 minute cycle. These patients most likely developed infection from which of the following bacteria?

- ☐ A. *Brucella melitensis*
- ☐ B. *Clostridium perfringens*
- ☐ C. *Escherichia coli*
- ☐ D. *Listeria monocytogenes*
- ☐ E. *Streptococcus pyogenes*

Submit









An epidemiologic study is conducted after a sudden increase in the rate of severe postoperative infections in a rural hospital. It is determined that all the patients who developed the infection were operated on with surgical instruments sterilized by a specific autoclave machine. The machine was found to be inadequately sterilizing the equipment due to a malfunction limiting the temperature to 100 C (212 F) during the 15 minute cycle. These patients most likely developed infection from which of the following bacteria?

- ☐ A. *Brucella melitensis* (5%)
- ✓ ☒ B. *Clostridium perfringens* (69%)
- ☐ C. *Escherichia coli* (12%)
- ☐ D. *Listeria monocytogenes* (7%)
- ☐ E. *Streptococcus pyogenes* (5%)

Correct

 69%  
Answered correctly 01 min, 32 secs  
Time Spent 02/10/2021  
Last Updated

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Autoclave machines are pressure cookers that use heated steam at temperatures of 134 C (273.2 F) to rapidly destroy pathogenic bacteria, fungi, viruses, and spores. Lower temperatures are often associated with inadequate sterilization due to the presence of **spore-forming bacteria**, which can survive at temperatures past the boiling point of water (100 C [212 F]). Bacterial spores are often found in soil and water and are resistant to chemical disinfectants, irradiation, desiccation, and temperatures as high as 120 C (248 F). **Bacillus** (eg, *Bacillus anthracis*) and **Clostridium** (eg, *Clostridium perfringens*, *C botulinum*) species are among the most common spore-forming pathogenic bacteria.

**(Choices A, C, D, and E)** These organisms do not form spores; vegetative bacteria are usually destroyed by temperatures >70 C (158 F).

### Educational objective:

Spore-forming bacteria can survive boiling temperatures. *Bacillus* and *Clostridium* species are common pathogenic spore-forming bacteria.

### References

- [Control of bacterial spores.](#)



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 52-year-old man is hospitalized due to 2 weeks of low-grade fever, malaise, anorexia, and fatigue. The patient has a history of bicuspid aortic valve and underwent aortic valve replacement a year ago. Physical examination reveals a new regurgitation murmur. Blood cultures repeatedly grow gram-positive cocci in clusters, which are identified as *Staphylococcus epidermidis*. This pathogen most likely demonstrates which of the following characteristics?

- ☐ A. Alpha hemolysis
- ☐ B. Mannitol fermentation
- ☐ C. Negative catalase test
- ☐ D. Negative coagulase test
- ☐ E. Novobiocin resistance
- ☐ F. Yellow pigment production

**Submit**

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Feedback

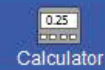
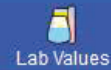


Suspend



End Block





A 52-year-old man is hospitalized due to 2 weeks of low-grade fever, malaise, anorexia, and fatigue. The patient has a history of bicuspid aortic valve and underwent aortic valve replacement a year ago. Physical examination reveals a new regurgitation murmur. Blood cultures repeatedly grow gram-positive cocci in clusters, which are identified as *Staphylococcus epidermidis*. This pathogen most likely demonstrates which of the following characteristics?

- ☐ A. Alpha hemolysis (3%)
- ☐ B. Mannitol fermentation (2%)
- ☐ C. Negative catalase test (6%)
- ☒ D. Negative coagulase test (78%)
- ☐ E. Novobiocin resistance (8%)
- ☐ F. Yellow pigment production (1%)

Correct



78%

Answered correctly



22 secs

Time Spent



10/10/2020

Last Updated

Block Time Remaining: 00:19:30

TUTOR

<https://t.me/USMLEWorldStep1>



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

***Staphylococcus epidermidis*** is a low-virulence skin commensal that rarely causes infection in healthy patients. However, those with prosthetic devices (eg, indwelling catheters, **artificial heart valves**, artificial joints) are at risk because the pathogen produces adhesion and biofilm proteins that allow it to grow on artificial surfaces. *S epidermidis* is one of the most common contaminants of blood cultures, but infection should be suspected when multiple blood cultures grow the bacteria and/or the patient has symptoms of clinical infection such as fever, malaise, and leukocytosis.

*Staphylococcus* species are gram-positive cocci that grow in **grape-like clusters**. They are differentiated from streptococci by the catalase test: Streptococci are catalase-negative whereas staphylococci are **catalase-positive (Choice C)**. Further speciation of staphylococci leverages the coagulase test (the ability to clot blood plasma), which differentiates *S aureus* from **coagulase-negative staphylococci** such as *S epidermidis*, *S haemolyticus*, and *S saprophyticus*.

**(Choice A)** Alpha hemolysis (partial, green hemolysis when plated on blood agar) is a feature of viridans streptococci, a common cause of infective endocarditis. Staphylococci species are either beta-hemolytic (complete hemolysis) or gamma-hemolytic (no hemolysis). *S epidermidis* is gamma-hemolytic.

**(Choice B)** *S aureus* and *S haemolyticus* can ferment mannitol, but *S epidermidis* cannot.

**(Choice E)** Novobiocin is an antibiotic that can be applied to plated colonies to differentiate *S*



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Feedback



Suspend



End Block



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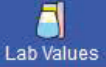
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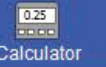
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Lab Values



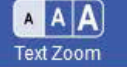
Notes



Calculator



Reverse Color



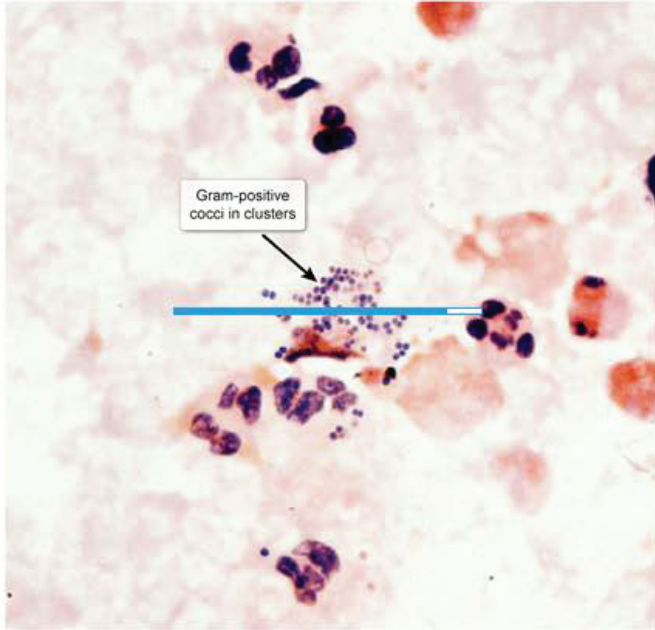
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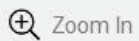
Settings

### Exhibit Display

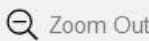
#### *Staphylococcus*



Gram-positive cocci in clusters



Zoom In



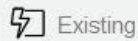
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(Choice E) Novobiocin is an antibiotic that can be applied to bared colonies to differentiate S

Block Time Remaining: 00:19:30

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<https://t.me/USMLEWorldStep1>



Feedback



Suspend



End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice A) Alpha hemolysis (partial, green hemolysis when plated on blood agar) is a feature of viridans streptococci, a common cause of infective endocarditis. Staphylococci species are either beta-hemolytic (complete hemolysis) or gamma-hemolytic (no hemolysis). *S epidermidis* is gamma-hemolytic.

(Choice B) *S aureus* and *S haemolyticus* can ferment mannitol, but *S epidermidis* cannot.

(Choice E) Novobiocin is an antibiotic that can be applied to plated colonies to differentiate *S saprophyticus* from other coagulase-negative *Staphylococcus* species: *S saprophyticus* is novobiocin-resistant whereas others, such as *S epidermidis*, are novobiocin-sensitive.

(Choice F) *S aureus* produces a golden-yellow surface pigment, which accounts for its name (*aureus* means gold in Latin). *S aureus* is a common cause of infective endocarditis and osteomyelitis, particularly in intravenous drug users.

### Educational objective:

*Staphylococcus epidermidis*, a gram-positive coccus that grows in clusters, is a skin commensal that is a common cause of infection in patients with prosthetic devices such as artificial joints or heart valves. Unlike *S aureus*, *S epidermidis* is coagulase-negative. Unlike *S saprophyticus* (another coagulase-negative staphylococci species), *S epidermidis* is susceptible to novobiocin.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 32-year-old man comes to the office for a follow-up appointment. The patient recently returned from a 10-day trip to Honduras. On the fifth day of his trip, he developed malaise, anorexia, and abdominal cramps, quickly followed by watery diarrhea. The patient had 5 or 6 stools daily but no fever. He took no medications and remained hydrated by drinking bottled water and soup. The patient felt better after 2 days and has had no additional symptoms since. He has no other medical conditions. Vital signs are within normal limits and the physical examination shows no abnormalities. Which of the following was most likely involved in producing this patient's gastrointestinal symptoms?

- ☐ A. Bacterial endotoxin
- ☐ B. Cholera-like enterotoxin
- ☐ C. Intestinal mucosal invasion
- ☐ D. Shiga-like toxin
- ☐ E. "Stacked-brick" intestinal adhesion

**Submit**

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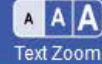
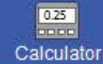
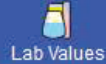
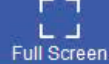
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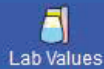


A 32-year-old man comes to the office for a follow-up appointment. The patient recently returned from a 10-day trip to Honduras. On the fifth day of his trip, he developed malaise, anorexia, and abdominal cramps, quickly followed by watery diarrhea. The patient had 5 or 6 stools daily but no fever. He took no medications and remained hydrated by drinking bottled water and soup. The patient felt better after 2 days and has had no additional symptoms since. He has no other medical conditions. Vital signs are within normal limits and the physical examination shows no abnormalities. Which of the following was most likely involved in producing this patient's gastrointestinal symptoms?

- ☐ A. Bacterial endotoxin (11%)
- ☒ B. Cholera-like enterotoxin (71%)
- ☐ C. Intestinal mucosal invasion (5%)
- ☐ D. Shiga-like toxin (6%)
- ☐ E. "Stacked brick" intestinal adhesion (4%)







Enterotoxigenic *Escherichia coli* (**ETEC**), a gram-negative, motile, enteric rod, is the most common cause of self-limited "**traveler's diarrhea**." Patients traveling to developing regions with poor sanitation are at greatest risk. Following ingestion, ETEC colonizes and adheres to small intestine enterocytes (mediated by pili). The subsequent elaboration of plasmid-encoded **heat-labile** (LT) and/or **heat-stable** (ST) **enterotoxin** results in the typical manifestations of abdominal cramping, nausea/vomiting, and (occasionally) low fever.

The **LT enterotoxin**, which **resembles cholera toxin** in structure and mode of action, increases intracellular cyclic AMP in gut mucosal cells by activating the stimulatory Gs membrane G protein, thereby activating adenylate cyclase. The ST enterotoxin is not inactivated by heat (likely due to its small molecular size); it causes an increase in cyclic GMP in the host cell cytoplasm by activating guanylate cyclase located on the apical membranes of host gut mucosal cells. As a result of both these enterotoxins, there is decreased reabsorption and increased secretion of sodium, water, and electrolytes, resulting in watery diarrhea.

**(Choice A)** Endotoxin is a lipopolysaccharide found in gram-negative bacteria that is released upon cell lysis. In the bloodstream, endotoxin causes a severe inflammatory response mediated by tumor necrosis factor-alpha and interleukin-1 secreted from activated macrophages.





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice A)** Endotoxin is a lipopolysaccharide found in gram-negative bacteria that is released upon cell lysis. In the bloodstream, endotoxin causes a severe inflammatory response mediated by tumor necrosis factor-alpha and interleukin-1 secreted from activated macrophages.

**(Choice C)** Intestinal invasion is a property of gastroenteritis caused by *Salmonella*, *Shigella*, enteroinvasive *E coli* (EIEC), and *Campylobacter jejuni*, as well as the protozoan *Entamoeba histolytica*. Invasion frequently leads to bloody or hemorrhagic diarrhea (due to mucosal cell necrosis).

**(Choice D)** Shiga-like toxin is produced by enterohemorrhagic *E coli* (EHEC) and shares many properties with Shiga toxin. It acts by inactivating the 60S ribosomal subunit in human cells, thereby inhibiting human cell protein production, leading to cell death. Patients with EHEC usually have bloody diarrhea due to mucosal cell death.

**(Choice E)** "Stacked-brick" intestinal adhesion is characteristic of enteroaggregative *E coli* (EAEC). These organisms adhere to human jejunal, ileal, and colonic mucosa in an aggregative, or stacked-brick, pattern and do not invade. EAEC is implicated in persistent diarrhea in infants in developing countries and in those with advanced immunosuppression (eg, AIDS).

### Educational objective:

Traveler's diarrhea is most frequently due to enterotoxigenic *Escherichia coli*. This pathogen produces







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

**(Choice D)** Shiga-like toxin is produced by enterohemorrhagic *E coli* (EHEC) and shares many properties with Shiga toxin. It acts by inactivating the 60S ribosomal subunit in human cells, thereby inhibiting human cell protein production, leading to cell death. Patients with EHEC usually have bloody diarrhea due to mucosal cell death.

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### Educational objective:

Traveler's diarrhea is most frequently due to enterotoxigenic *Escherichia coli*. This pathogen produces plasmid-encoded, heat-labile (LT, cholera-like) and heat-stable (ST) enterotoxins. LT activates adenylate cyclase, leading to increased intracellular cyclic AMP; ST activates guanylate cyclase leading to increased intracellular cyclic GMP. Both cause water and electrolyte loss and watery diarrhea.

### References

- Cholera-like enterotoxins and regulatory T cells.



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Feedback

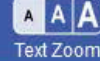
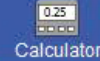
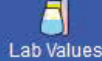
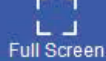


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End Block





A 19-year-old man comes to the physician due to diarrhea for the last 4 months. He visited a student health clinic at his university a month ago and was prescribed a course of antibiotics, but his diarrhea failed to improve. He also has persistent nausea, a bloating sensation, and a 6.8-kg (15-lb) weight loss. Microscopic examination of his stool for ova and parasites following trichrome staining is shown in the [exhibit](#). Impairment of which of the following immune functions would most likely predispose to this patient's infection?

- ☐ A. Bacterial killing by neutrophils
- ☐ B. CD8+ T lymphocyte-mediated cytotoxicity
- ☐ C. Eosinophil-mediated cytotoxicity
- ☐ D. Membrane attack complex formation
- ☐ E. Secretory IgA production

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Full Screen



Tutorial



Lab Values



Notes



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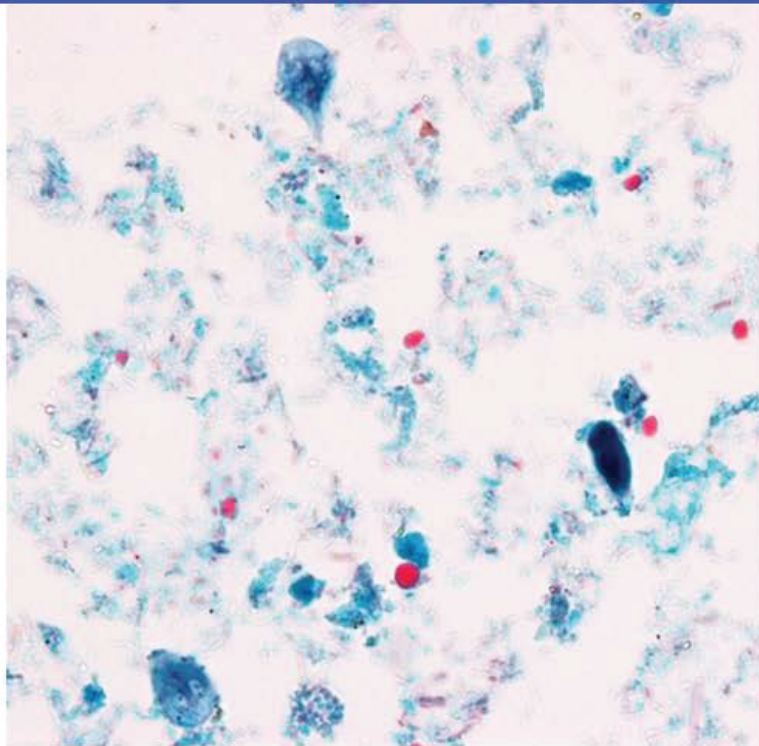
A 19-year-old male patient presents to a health clinic at the local community center to improve. He has a history of chronic cough and sputum production. Microscopic examination of the sputum reveals the following exhibit. Impaired patient's infection is most likely due to:

- ☐ A. Bacteria
- ☐ B. CD8+ T cells
- ☐ C. Eosinophils
- ☐ D. Macrophages
- ☐ E. Secretory cells

Submit

Block Time Remaining  
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### Exhibit Display



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A 19-year-old man comes to the physician due to diarrhea for the last 4 months. He visited a student health clinic at his university a month ago and was prescribed a course of antibiotics, but his diarrhea failed to improve. He also has persistent nausea, a bloating sensation, and a 6.8-kg (15-lb) weight loss. Microscopic examination of his stool for ova and parasites following trichrome staining is shown in the [exhibit](#). Impairment of which of the following immune functions would most likely predispose to this patient's infection?

- ☐ A. Bacterial killing by neutrophils
- ☐ B. CD8+ T lymphocyte-mediated cytotoxicity
- ☐ C. Eosinophil-mediated cytotoxicity
- ☐ D. Membrane attack complex formation
- ☐ E. Secretory IgA production

Submit







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Previous



Next



Full Screen



Tutorial



Lab Values



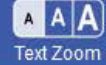
Notes



Calculator



Reverse Color



Text Zoom



Settings

A 19-year-old man comes to the physician due to diarrhea for the last 4 months. He visited a student health clinic at his university a month ago and was prescribed a course of antibiotics, but his diarrhea failed to improve. He also has persistent nausea, a bloating sensation, and a 6.8-kg (15-lb) weight loss. Microscopic examination of his stool for ova and parasites following trichrome staining is shown in the exhibit. Impairment of which of the following immune functions would most likely predispose to this patient's infection?

- ☐ A. Bacterial killing by neutrophils (1%)
- ☐ B. CD8+ T lymphocyte-mediated cytotoxicity (7%)
- ☐ C. Eosinophil-mediated cytotoxicity (28%)
- ☐ D. Membrane attack complex formation (2%)
- ☒ E. Secretory IgA production (60%)

Correct

60%  
Answered correctly

49 secs  
Time Spent

11/30/2020  
Last Updated

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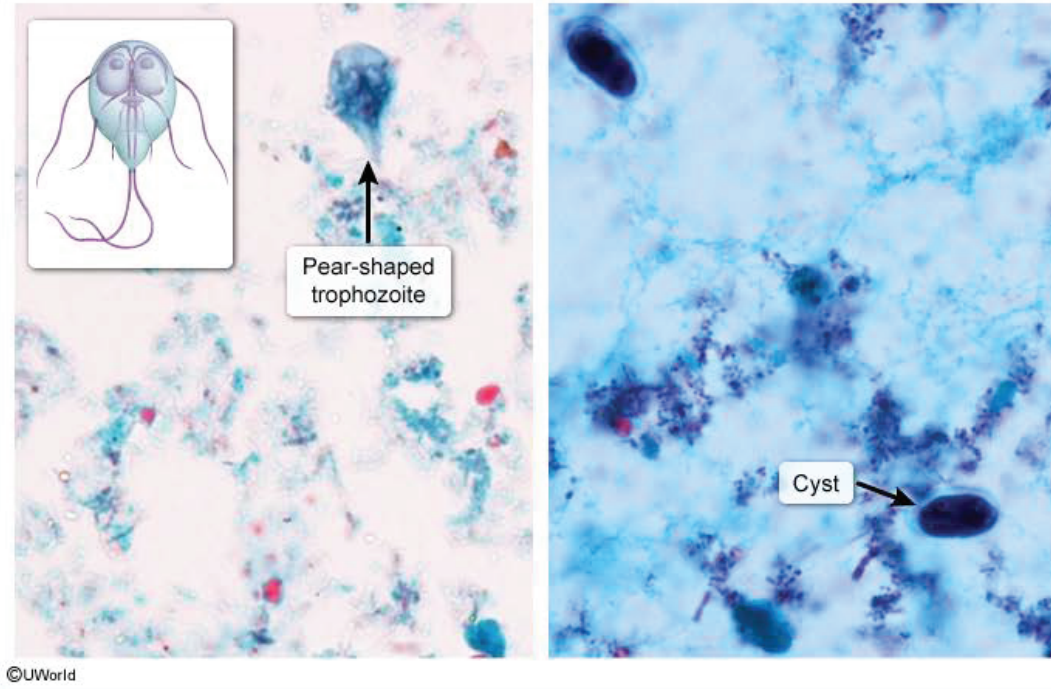


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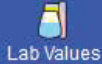
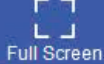


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## Giardia



***Giardia lamblia*** is an intestinal flagellate that exists in 2 forms: a trophozoite (pathogenic stage) or a cyst



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***Giardia lamblia*** is an intestinal flagellate that exists in 2 forms: a trophozoite (pathogenic stage) or a cyst (infective stage). The trophozoite is a bilaterally symmetric, **pear-shaped** organism with multiple flagella and 2 nuclei (owl's eyes appearance); the cysts are oval and contain up to 4 nuclei. The disease is transmitted by drinking contaminated water (eg, campers, travelers to endemic areas) or via fecal-oral transmission (eg, children in day care centers).

Giardiasis can be asymptomatic or present with a variable combination of **diarrhea**, nausea, abdominal cramps, and fat malabsorption (eg, foul-smelling stools). The diagnosis is confirmed by **stool microscopy for ova and parasites** or fecal immunoassays for *Giardia* antigens. Small-bowel biopsy is sometimes performed when stool studies are nondiagnostic and can show varying degrees of **villous atrophy** and crypt hyperplasia depending on disease severity.

Immune defence against *Giardia* involves CD4+ T helper cell induction of **secretory IgA production**. Secretory IgA helps prevent and clear infection by binding to trophozoites and impairing their adherence to the upper small-bowel mucosa. Children with IgA deficiency, X-linked agammaglobulinemia, and common variable immune deficiency have a predisposition to developing chronic giardiasis.

**(Choices A and D)** Neutrophils and the complement system are important defense mechanisms against







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

the upper small-bowel mucosa. Children with IgA deficiency, X-linked agammaglobulinemia, and common variable immune deficiency have a predisposition to developing chronic giardiasis.

**(Choices A and D)** Neutrophils and the complement system are important defense mechanisms against bacterial infections. They have no significant role in controlling parasitic infections.

**(Choice B)** CD8+ T cells are not important in clearing giardiasis; they are more important for combating intracellular intestinal pathogens such as *Cryptosporidium parvum* and *Toxoplasma gondii*.

**(Choice C)** Eosinophils do not play an important role in immune defense against *Giardia*; eosinophilia is not seen in giardiasis and white cells are usually absent from the stool. Eosinophils are more important for combating intestinal helminthic infections.

### Educational objective:

*Giardia lamblia* causes injury to the duodenal and jejunal mucosa by adhering to the intestinal brush border and releasing molecules that induce a mucosal inflammatory response. Secretory IgA, which impairs adherence, is the major component of adaptive immunity against *G lamblia* infection. Conditions causing IgA deficiency predispose patients to chronic giardiasis.

Microbiology

Microbiology (General Principles)

Giardia

Block Time Remaining: 00:21:21

TUTOR

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1



Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 35-year-old man is found to have elevated alanine aminotransferase and aspartate aminotransferase levels. He has no abdominal pain, nausea, or vomiting. The patient has used intravenous drugs in the past but denies significant alcohol use. His past medical history is negative for blood transfusions or excessive acetaminophen use. Physical examination findings are normal. Laboratory studies show high titers of IgG directed against the hepatitis C envelope protein. Which of the following is the most likely reason that these antibodies do not confer effective immunity against the infection?

- ☐ A. Envelope proteins are lost after recurrent viral replication
- ☐ B. Envelope proteins are sequestered within hepatocytes
- ☐ C. Envelope proteins have low immunogenicity
- ☐ D. Envelope proteins have variations in their antigenic structure
- ☐ E. The antibodies do not have neutralizing properties

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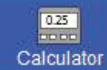
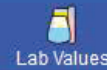
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A 35-year-old man is found to have elevated alanine aminotransferase and aspartate aminotransferase levels. He has no abdominal pain, nausea, or vomiting. The patient has used intravenous drugs in the past but denies significant alcohol use. His past medical history is negative for blood transfusions or excessive acetaminophen use. Physical examination findings are normal. Laboratory studies show high titers of IgG directed against the hepatitis C envelope protein. Which of the following is the most likely reason that these antibodies do not confer effective immunity against the infection?

- ☐ A. Envelope proteins are lost after recurrent viral replication (5%)
- ☐ B. Envelope proteins are sequestered within hepatocytes (10%)
- ☐ C. Envelope proteins have low immunogenicity (10%)
- ☒ D. Envelope proteins have variations in their antigenic structure (68%)
- ☐ E. The antibodies do not have neutralizing properties (5%)

Correct

 68%  
Answered correctly 38 secs  
Time Spent 03/06/2021  
Last Updated

Block Time Remaining: 00:21:59

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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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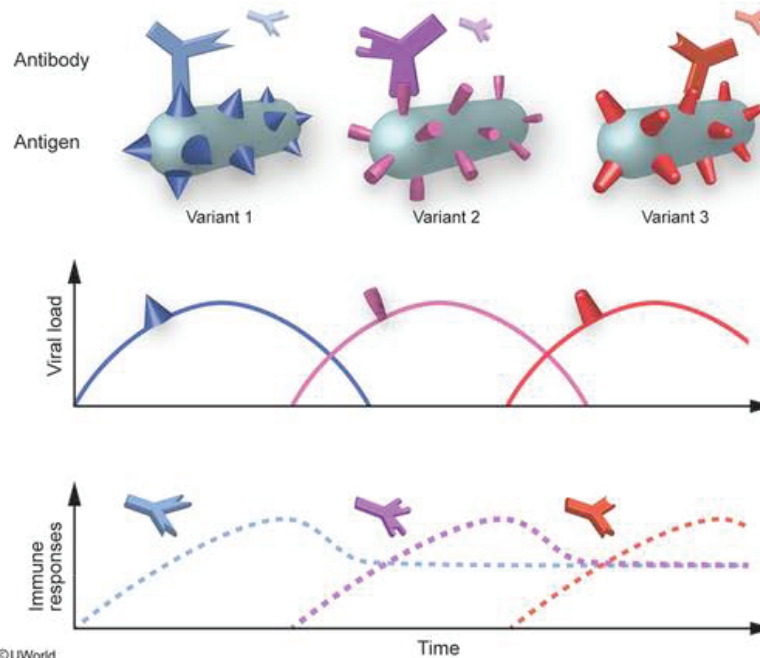
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### Exhibit Display

#### Antigenic variation



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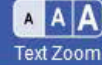
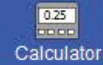
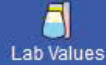
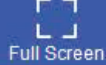
**Hepatitis C virus (HCV)** has 6 or more genotypes and multiple subtypes that differ in genomic composition by as much as 30%-35%. This is largely due to the fact that the virion-encoded **RNA-dependent RNA polymerase** has **no proofreading** 3' → 5' exonuclease activity, which results in many errors during replication.

Although most patients are infected with a single genotype, the high mutation rate leads to the development of distinct quasispecies within infected individuals over time. These variant strains differ primarily at **hypervariable genomic regions**, such as those found in the sequences coding for its **envelope glycoproteins**. The continuous generation of novel envelope glycoproteins prevents infected individuals from mounting an effective immune response. As production of host antibodies against a quasispecies commences, that strain dies off and new ones take its place. The tremendous antigenic variety of HCV has significantly slowed efforts to develop an effective vaccine.

**(Choices A and B)** The envelope proteins of HCV are not lost after recurrent viral replication nor are they sequestered within hepatocytes. These proteins are necessary for viral infectivity as they mediate membrane adhesion and fusion with host hepatocytes.

**(Choice C)** Like most foreign (nonself) proteins, the envelope proteins of HCV are highly immunogenic.





**(Choices A and B)** The envelope proteins of HCV are not lost after recurrent viral replication nor are they sequestered within hepatocytes. These proteins are necessary for viral infectivity as they mediate membrane adhesion and fusion with host hepatocytes.

**(Choice C)** Like most foreign (nonself) proteins, the envelope proteins of HCV are highly immunogenic.

**(Choice E)** Host antibodies against HCV have neutralizing properties and are effective in eliminating more established hepatitis C quasispecies. It is the constantly emerging mutant strains that pose the greatest challenge to the host immune system.

### Educational objective:

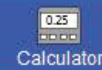
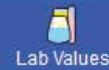
Genetic variations created during hepatitis C virus (HCV) replication result in marked variety in the antigenic structure of HCV envelope proteins. The production of host antibodies lags behind that of new mutant HCV strains, preventing infected individuals from mounting an effective immune response.

### References

- [Virus-neutralizing antibodies to hepatitis C virus.](#)
- [Hepatitis C virus hypervariable region 1 modulates receptor interactions, conceals the CD81 binding site, and protects conserved neutralizing epitopes.](#)







A 41-year-old woman comes to the emergency department due to 2 days of severe shortness of breath, high fevers, cough, and myalgias. The patient is a businesswoman who works in the poultry industry. She recently returned from a trip to China, where she visited several factories in different parts of the country. Her temperature is 39.1 C (102.4 F). The patient is in respiratory distress, and crackles and diffuse wheezes are present on pulmonary examination. Laboratory results show that she contracted an orthomyxovirus that was responsible for an upper respiratory infection epidemic in China. Transmission of the virus was originally thought to occur only through contact with poultry, but during the outbreak, sustained human-to-human transmission was observed. Which of the following is most likely responsible for the infectivity of this virus in humans?

- ☐ A. Antigenic drift
- ☐ B. Complementation
- ☐ C. Frameshift mutation
- ☐ D. Genetic reassortment
- ☐ E. Phenotypic mixing





recently returned from a trip to China, where she visited several factories in different parts of the country. Her temperature is 39.1 C (102.4 F). The patient is in respiratory distress, and crackles and diffuse wheezes are present on pulmonary examination. Laboratory results show that she contracted an **orthomyxovirus** that was responsible for an upper respiratory infection epidemic in China. Transmission of the virus was originally thought to occur only through contact with poultry, but during the outbreak, sustained human-to-human transmission was observed. Which of the following is most likely responsible for the infectivity of this virus in humans?

- ☐ A. Antigenic drift (22%)
- ☐ B. Complementation (0%)
- ☐ C. Frameshift mutation (1%)
- ☒ D. Genetic reassortment (67%)
- ☐ E. Phenotypic mixing (7%)

Correct

67%



01 min, 23 secs



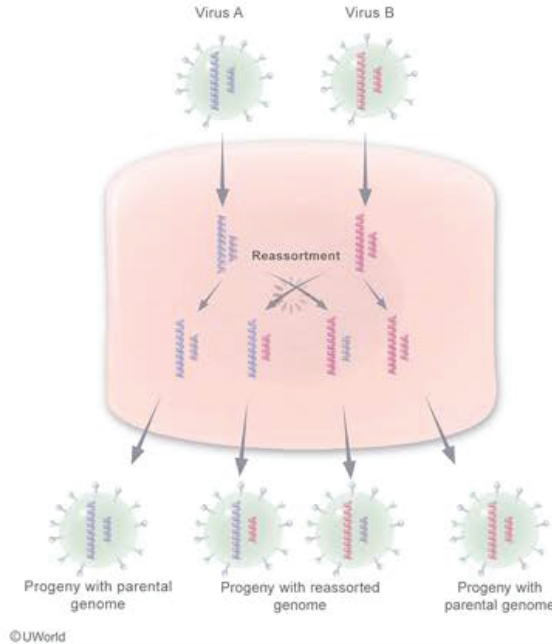
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### Exhibit Display

#### Reassortment (segmented viruses)



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**Influenza viruses (orthomyxoviruses)** are respiratory pathogens that can affect several species, including **humans, birds, and swine**. They possess the surface proteins hemagglutinin (HA) and neuraminidase (NA), which are virulence factors required for infectivity. These proteins are also targets of the immune system, and neutralizing antibodies against them can confer immunity to specific influenza strains. As such, HA and NA are under constant selective pressure both to maintain species-specific virulence and evade immune recognition.

Orthomyxoviruses contain a **segmented** genome, and HA and NA are coded by separate RNA segments. This allows for **genetic reassortment** when 2 distinct strains infect the same cell. For instance, avian coinfection with a human influenza A virus (which can also infect birds, the reservoir species for all influenza A subtypes) and an animal influenza A virus can lead to the human-type HA and the animal-type NA being packaged together into the same virion. This has the potential to create a **novel strain** of virus to which **humans are susceptible** but have **no immunologic resistance**. This phenomenon is known as antigenic shift, and is responsible for the majority of pandemics and epidemics of influenza A.

**(Choice A)** Antigenic drift refers to point mutations in HA and NA genes that slightly alter the product proteins, allowing them to evade immune recognition and possibly increasing infectivity of the virus.

However, a change in species-to-species transmission likely represents a major modification in protein





**(Choice A)** Antigenic drift refers to point mutations in HA and NA genes that slightly alter the product proteins, allowing them to evade immune recognition and possibly increasing infectivity of the virus. However, a change in species-to-species transmission likely represents a major modification in protein structure that is better explained by RNA segment reassortment.

**(Choice B)** In genetics, complementation occurs when 2 different strains of a mutant organism are able to produce wild-type offspring. Typically, both parents have homozygous mutations in different genes within the same metabolic pathway. When they are crossed, the offspring inherits 1 normal allele from each parent, allowing them to bypass both of the metabolic blockades and display the wild-type phenotype.

**(Choice C)** Frameshift mutations result when a number of bases that are **not** a multiple of 3 are added to or deleted from the coding region of a gene. This typically results in premature termination of translation and a truncated protein containing the wrong amino acids.

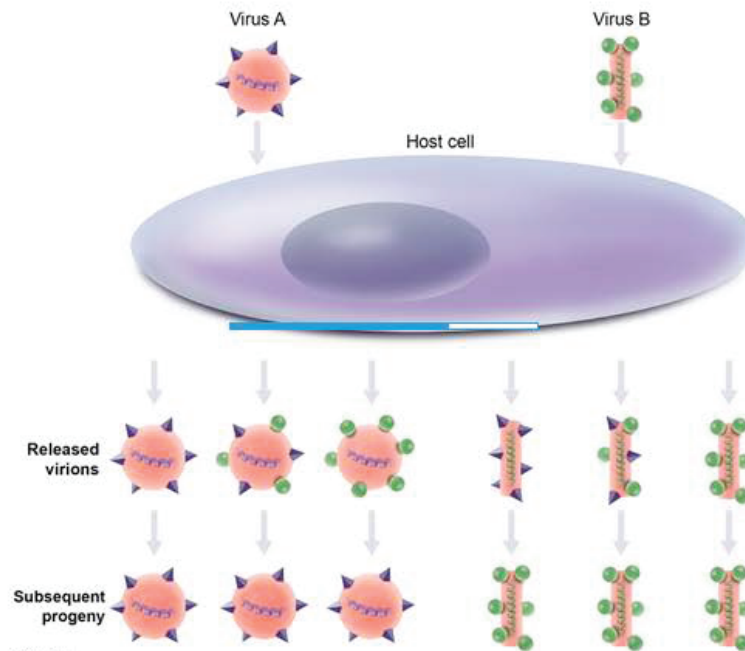
**(Choice E)** **Phenotypic mixing** occurs when 2 viruses infect the same cell and progeny viruses exhibit coat or envelope proteins not coded for by the genetic material packaged within them. However, subsequent progeny express only the proteins encoded by their genome. The above scenario is not an example of phenotypic mixing as human-to-human transmission was sustained.

**Educational objective:**



### Exhibit Display

#### Phenotypic mixing



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**Educational objective.**

Block Time Remaining: 00:23:22

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1



Feedback



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End Block





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

parent, allowing them to bypass both of the metabolic blockades and display the wild-type phenotype.

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### Educational objective:

Influenza epidemics and pandemics are typically caused by reassortment of the RNA segments coding for hemagglutinin or neuraminidase proteins (major antigenic shifts). This process can occur between human and animal strains of influenza A virus in avian or swine hosts.

Microbiology  
Subject

Microbiology (General Principles)  
System

Viral genetics  
Topic

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Feedback

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5

6

7

8

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10

11

12

13

14

15

16

17

18

19

20

21

22

23

24

25

26

27

28

29

30



Item 23 of 31

Question Id: 107



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 30-year-old man is admitted to the intensive care unit after his wife found him unconscious at home. She says that he has lost a significant amount of weight recently despite no significant change in dietary habits. Laboratory studies show a serum pH of 7.1 and positive serum ketones. His mucous membranes are extremely dry. Treatment is initiated, and the patient's condition improves. However, he now has fever, headache, and eye pain. Examination of the nasal cavity shows a black necrotic eschar adherent to the inferior turbinate. Which of the following procedures would most likely reveal the pathogen responsible for this patient's infection?

- ☐ A. Blood cultures
- ☐ B. Lumbar puncture
- ☐ C. Mucosal biopsy
- ☒ D. Ophthalmoscopy
- ☐ E. Serologic testing
- ☐ F. Skin hypersensitivity test

Block Time Remaining: 00:23:23

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Feedback



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says that he has lost a significant amount of weight recently despite no significant change in dietary habits.

Laboratory studies show a serum pH of 7.1 and positive serum ketones. His mucous membranes are extremely dry. Treatment is initiated, and the patient's condition improves. However, he now has fever, headache, and eye pain. Examination of the nasal cavity shows a black necrotic eschar adherent to the inferior turbinate. Which of the following procedures would most likely reveal the pathogen responsible for this patient's infection?

- ☐ A. Blood cultures (20%)
- ☐ B. Lumbar puncture (9%)
- ☒ C. Mucosal biopsy (61%)
- ☐ D. Ophthalmoscopy (1%)
- ☐ E. Serologic testing (6%)
- ☐ F. Skin hypersensitivity test (0%)

Correct

61%



52 secs



11/12/2020

Block Time Remaining: 00:24:14

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Feedback

Suspend

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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Settings

Facial pain, headache, and nasal eschar in a patient with likely diabetic ketoacidosis (pH 7.1, positive ketones, and dry mucous membranes in a young patient with recent unintended weight loss) are highly suggestive of **mucormycosis**, caused by *Mucor* or *Rhizopus*, among others. Most cases are **rhinocerebral**; the infection (acquired by spore inhalation) ascends from the nasal passage to the sinuses/orbits and then sometimes to the brain, leading to confusion, neurological deficits, and death. The increased incidence of mucormycosis in patients with **diabetes mellitus** is due to the ketone reductase activity of *Rhizopus*, allowing it to thrive in ketoacidotic environments.

Histologic examination (eg, **mucosal biopsy**) is necessary for diagnosis. The **fungi** appear as ribbon-like **broad nonseptate hyphae** with **right-angle branching**. Tissue invasion is seen along blood vessels; vascular thrombosis and tissue necrosis can occur. A black **necrotic eschar** in the nasal cavity is characteristic. Management includes amphotericin B and surgical debridement.

Mucormycosis (common in diabetes) must be differentiated from invasive aspergillosis causing rhinosinusitis (common in neutropenic patients). On light microscopy, *Aspergillus* is seen as **septated narrow hyphae with sharp-angle branching**.

**(Choice A)** Blood cultures are usually negative in mucormycosis despite the organism's angioinvasive nature. In contrast, blood cultures can be useful in diagnosing candidemia, which has a variable clinical



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Suspend



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Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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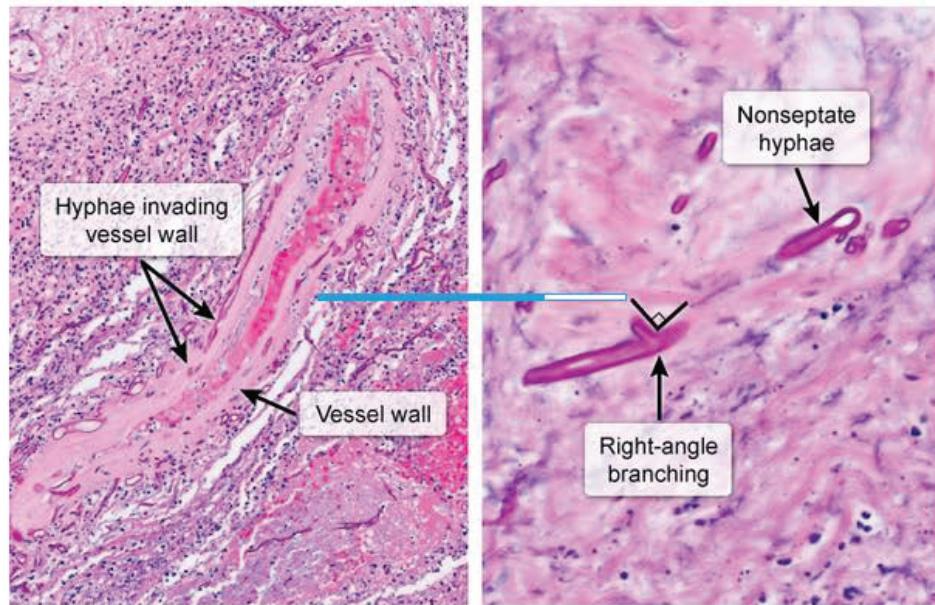
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## Exhibit Display

## Mucormycosis



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Block Time Remaining: 00:24:14

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Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



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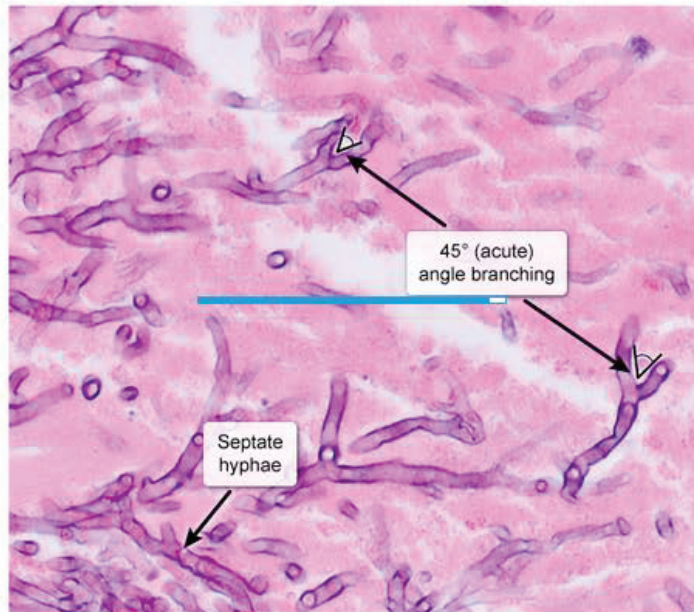


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## Exhibit Display

*Aspergillus*

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Block Time Remaining: 00:24:14

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Feedback



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narrow hyphae with sharp-angle branching.

**(Choice A)** Blood cultures are usually negative in mucormycosis despite the organism's angioinvasive nature. In contrast, blood cultures can be useful in diagnosing candidemia, which has a variable clinical presentation ranging from low-grade fever to severe sepsis with multiorgan failure.

**(Choice B)** Lumbar puncture helps to diagnose cryptococcal meningitis, a fungal infection that typically has an indolent presentation and usually affects patients with AIDS. India ink staining of cerebrospinal fluid reveals the classic encapsulated yeast of *Cryptococcus neoformans*.

**(Choice D)** Ophthalmoscopy is useful for the diagnosis of *Candida* endophthalmitis, which typically presents with impaired visual acuity.

**(Choices E and F)** Serologic testing is important in the diagnosis of allergic bronchopulmonary aspergillosis (ABPA), where increased titers of IgE and antibodies to *Aspergillus fumigatus* are seen. Skin hypersensitivity testing is also useful. However, the typical presentation of ABPA is recurrent episodes of fever and bronchial obstruction in a patient with asthma.

**Educational objective:**

Facial pain, headache, and a black necrotic eschar in the nasal cavity of a patient with diabetic ketoacidosis are highly suggestive of mucormycosis. Histologic examination of the affected tissue is





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

**(Choice B)** Lumbar puncture helps to diagnose cryptococcal meningitis, a fungal infection that typically has an indolent presentation and usually affects patients with AIDS. India ink staining of cerebrospinal fluid reveals the classic encapsulated yeast of *Cryptococcus neoformans*.

**(Choice D)** Ophthalmoscopy is useful for the diagnosis of *Candida* endophthalmitis, which typically presents with impaired visual acuity.

**(Choices E and F)** Serologic testing is important in the diagnosis of allergic bronchopulmonary aspergillosis (ABPA), where increased titers of IgE and antibodies to *Aspergillus fumigatus* are seen. Skin hypersensitivity testing is also useful. However, the typical presentation of ABPA is recurrent episodes of fever and bronchial obstruction in a patient with asthma.

### Educational objective:

Facial pain, headache, and a black necrotic eschar in the nasal cavity of a patient with diabetic ketoacidosis are highly suggestive of mucormycosis. Histologic examination of the affected tissue is necessary to confirm the diagnosis. The fungi show broad nonseptate hyphae with right-angle branching. Treatment consists of surgical debridement and antifungal therapy.

### References

- [Novel perspectives on mucormycosis: pathophysiology, presentation, and management.](#)



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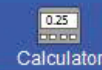
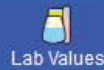
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The influenza A virus uses a sialic acid as a receptor for cellular entry. The chemical composition of the specific type of sialic acid that the virus interacts with differs among animal species. The avian influenza virus attaches to a specific sialic acid that is present in fowl epithelial cells but absent in human cells, whereas the human influenza virus can only attach to the type of sialic acid present in human respiratory epithelium. When pig epithelial cells, which contain both types of sialic acid, are infected with the combination of avian and human influenza A viruses, some of the new avian influenza viral particles become capable of attaching to human cells. However, the progeny of this new strain of avian influenza virus is still unable to attach to human epithelial cells. Which of the following phenomena best describes the change in the avian influenza virus in this experiment?

- ☐ A. Interference
- ☐ B. Phenotypic mixing
- ☐ C. Reassortment
- ☐ D. Recombination
- ☐ E. Transformation







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



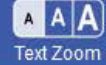
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virus attaches to a specific sialic acid that is present in fowl epithelial cells but absent in human cells, whereas the human influenza virus can only attach to the type of sialic acid present in human respiratory epithelium. When pig epithelial cells, which contain both types of sialic acid, are infected with the combination of avian and human influenza A viruses, some of the new avian influenza viral particles become capable of attaching to human cells. However, the progeny of this new strain of avian influenza virus is still unable to attach to human epithelial cells. Which of the following phenomena best describes the change in the avian influenza virus in this experiment?

- ☐ A. Interference (1%)
- ☒ B. Phenotypic mixing (42%)
- ☐ C. Reassortment (32%)
- ☐ D. Recombination (12%)
- ☐ E. Transformation (9%)

Correct



42%

Answered correctly



01 min, 18 secs

Time spent



01/26/2021

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Block Time Remaining: 00:25:32

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Mark

Previous  
Virus A

Next

Full Screen

Tutorial

Lab Values

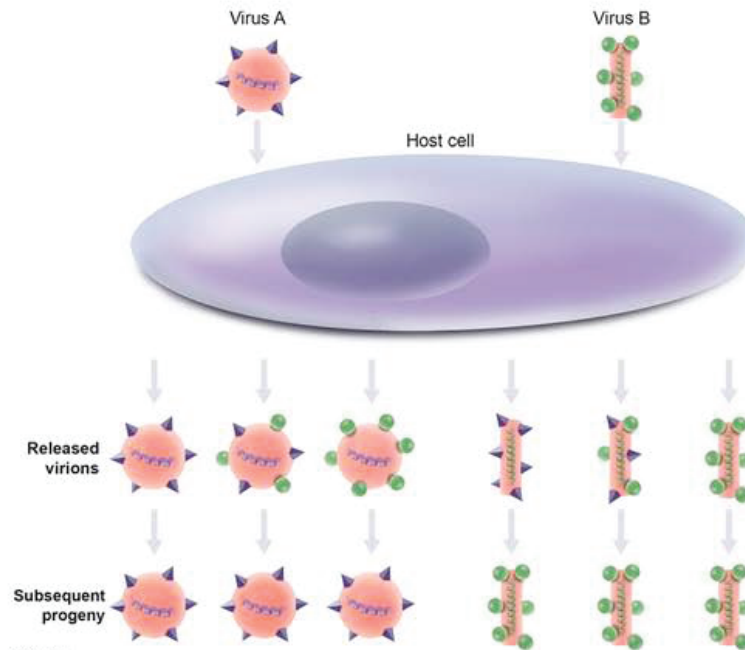
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Exhibit Display  
Phenotypic mixing

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End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



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The acquisition of a new viral surface protein is often all that is necessary for a virus to infect a new type of host cell. In this scenario, avian and human influenza virus particles infect host pig cells; certain progeny avian virus particles obtain some of the surface components (eg, sialic acid receptors) of the human influenza virus, allowing the avian virus to infect human cells. This exchange is an example of **phenotypic mixing**, which generally occurs when a host cell is coinfecting with 2 viral strains and progeny virions contain **unchanged parental genome** from one strain and **nucleocapsid (or envelope) proteins** from the **other** strain. However, because there is no change in the underlying viral genomes (no genetic exchange), subsequent progeny will **revert** to having only avian influenza type surface proteins and will again be noninfectious to human epithelium.

**(Choice A)** Interference occurs when one virus inhibits replication and/or release of a second virus that is infecting the same cell. Simple interference would not result in a new phenotype for progeny.

**(Choice C)** Reassortment refers to changes in genomic composition that occur when host cells are coinfecting with 2 segmented viruses that exchange whole genome segments. When reassortment takes place in a cell coinfecting by 2 viral strains, any genomic change in first generation progeny will also be present in subsequent progeny.

**(Choice D)** Recombination may be defined as the exchange of genes between 2 chromosomes (double

Block Time Remaining: 00:25:32

<https://t.me/USMLEWorldStep1>

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Feedback



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place in a cell coinfecting by 2 viral strains, any genomic change in first generation progeny will also be present in subsequent progeny.

**(Choice D)** Recombination may be defined as the exchange of genes between 2 chromosomes (double-stranded DNA molecules) by crossing over within homologous regions. As is the case with reassortment, any genomic change in the first generation progeny will also be present in subsequent progeny.

**(Choice E)** Transformation is generally defined as naked DNA uptake by a prokaryotic or eukaryotic cell. In virology, this term may also describe incorporation of viral DNA into a host cell chromosome. Transformation alters the genetic composition of the host cell but typically causes no genomic change in progeny virions.

### Educational objective:

Phenotypic mixing refers to coinfection of a host cell by 2 viral strains, resulting in progeny virions that contain nucleocapsid proteins from one strain and the unchanged parental genome of the other strain. Because there is no change in the underlying viral genomes (no genetic exchange), the next generation of virions revert to their original, unmixed phenotypes.

Microbiology

Microbiology (General Principles)

Viral genetics

Subject

System

Topic

Block Time Remaining: 00:25:32

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Feedback



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End Block

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A 22-year-old man with fever and joint pain is found to have atypical lymphocytes on his blood smear. Further evaluation shows that his condition is caused by an enveloped virus containing partially double-stranded circular DNA. An enzyme packed in its virion has RNA-dependent DNA-polymerase activity. This patient is most likely infected with which of the following viruses?

- ☐ A. Coxsackie virus
- ☐ B. Cytomegalovirus
- ☐ C. Epstein-Barr virus
- ☐ D. Hepatitis B virus
- ☐ E. Human immunodeficiency virus
- ☐ F. Parvovirus B19

Submit





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

A 22-year-old man with fever and joint pain is found to have atypical lymphocytes on his blood smear. Further evaluation shows that his condition is caused by an enveloped virus containing partially double-stranded circular DNA. An enzyme packed in its virion has RNA-dependent DNA-polymerase activity. This patient is most likely infected with which of the following viruses?

- ☐ A. Coxsackie virus (2%)
- ☐ B. Cytomegalovirus (5%)
- ☐ C. Epstein-Barr virus (23%)
- ☒ D. Hepatitis B virus (55%)
- ☐ E. Human immunodeficiency virus (7%)
- ☐ F. Parvovirus B19 (5%)

Correct

55%  
Answered correctly31 secs  
Time Spent12/02/2020  
Last Updated

Block Time Remaining: 00:26:03

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Feedback

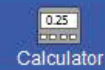
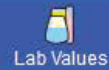


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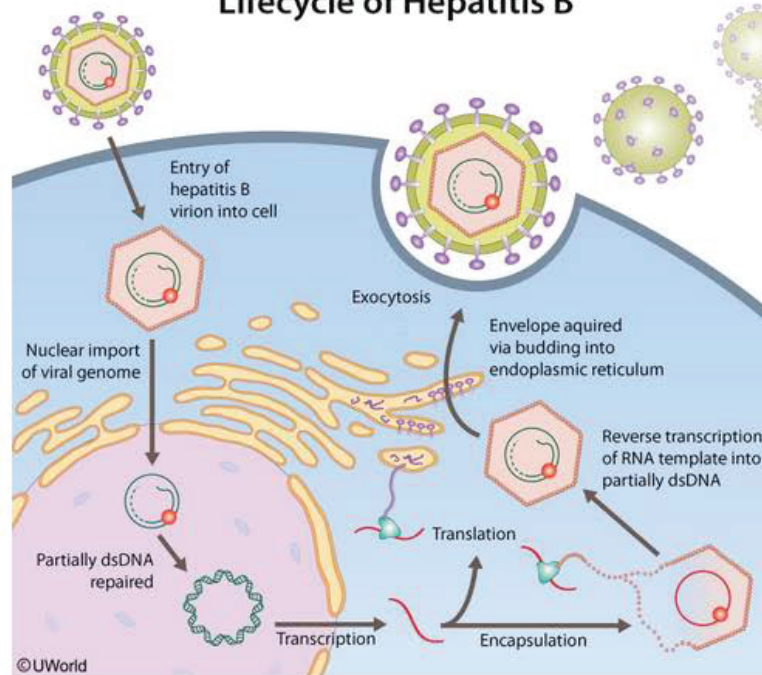
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## Exhibit Display

## Lifecyle of Hepatitis B



Zoom In



Zoom Out



Reset



New



Existing



My Notebook

Block Time Remaining: 00:26:03

<https://t.me/USMLEWorldStep1>

Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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This patient's fever and joint pain are nonspecific symptoms of a viral infection. Atypical (reactive) lymphocytes are also nonspecific and are seen with many viral infections (although Epstein-Barr virus and cytomegalovirus usually present with the highest counts).

Based on the described viral morphology, this patient is most likely infected with the hepatitis B virus (HBV), a member of the DNA-containing *Hepadnaviridae* family. The mature virion (called a Dane particle) consists of a hexagonal protein core (capsid) covered with a lipid bilayer envelope studded with proteins and carbohydrates. The HBV genome is a partially double-stranded circular DNA molecule housed within the capsid.

After the virion enters the cell, the capsid is released into the cytoplasm and the viral genome is transferred into the nucleus. The viral DNA is then repaired to form a fully double-stranded circular minichromosome that is capable of being transcribed into viral mRNAs. Replication of the genome occurs within a newly synthesized capsid containing the full-length viral mRNA transcript. Reverse transcriptase (which has both RNA- and DNA-dependent DNA-polymerase activity) acts on this RNA template to create a single-stranded DNA intermediate that is then converted back into circular, partially double-stranded DNA. The mature capsid is then enveloped by a portion of the endoplasmic reticulum containing virally-coded proteins to form



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

capsid is then enveloped by a portion of the endoplasmic reticulum containing virally-coded proteins to form the completed virion.

**(Choice A)** Coxsackie virus is within the *Picornaviridae* family and is composed of an icosahedral nucleocapsid and a + single-stranded RNA genome. The RNA has a protein on the 5' end that acts as a primer for transcription by RNA-dependent RNA polymerase.

**(Choices B and C)** Cytomegalovirus and Epstein-Barr virus are members of the *Herpesviridae* family. All viruses within this family contain an icosahedral core surrounded by a lipoprotein envelope and have double-stranded, linear DNA. These are the only viruses to acquire their envelopes by budding from the nuclear membrane.

**(Choice E)** Human immunodeficiency virus is within the *Lentivirus* subgroup of retroviruses. It contains a bar-shaped protein core surrounded by a glycoprotein envelope that includes the gp120 and gp41 glycoproteins. The genome is diploid, consisting of 2 + single-stranded RNA molecules that are transcribed into double-stranded DNA by a reverse transcriptase present in the capsid.

**(Choice F)** Parvovirus B19 is a small nonenveloped icosahedral virus with a linear, single-stranded DNA genome. There is no polymerase in the virion.

**Educational objective:**

Block Time Remaining: 00:26:03

<https://t.me/USMLEWorldStep1>



Feedback

Suspend

End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

nuclear membrane.

**(Choice E)** Human immunodeficiency virus is within the *Lentivirus* subgroup of retroviruses. It contains a bar-shaped protein core surrounded by a glycoprotein envelope that includes the gp120 and gp41 glycoproteins. The genome is diploid, consisting of 2 + single-stranded RNA molecules that are transcribed into double-stranded DNA by a reverse transcriptase present in the capsid.

**(Choice F)** Parvovirus B19 is a small nonenveloped icosahedral virus with a linear, single-stranded DNA genome. There is no polymerase in the virion.

### Educational objective:

Replication of the hepatitis B genome occurs within a newly synthesized capsid through the action of reverse transcriptase on an RNA template. The mature capsid contains partially double-stranded circular DNA and reverse transcriptase.

### References

- [Molecular virology of hepatitis B virus for clinicians.](#)

Microbiology

Microbiology (General Principles)

Hepatitis b

Subject

System

Topic

Block Time Remaining: 00:26:03

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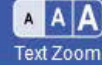
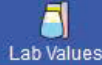
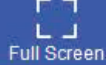
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Microbiology researchers conduct a series of experiments to determine how pathogenicity is transmitted among different strains of *Streptococcus pneumoniae*. In the first experiment, they inject nonvirulent strain A into the peritoneal cavity of laboratory mice and observe no ill effects. In the second experiment, researchers subject virulent strain B to a detergent agent that kills and lyses the bacterial cells. They then inject the lysate into the peritoneal cavity of a new group of mice and again observe no ill effects. During a third experiment, they inject live strain A bacteria in combination with the killed strain B lysate, resulting in death of the mice. Which of the following genetic processes most likely accounts for the observed findings of these experiments?

- ☐ A. Direct uptake of extracellular DNA
- ☐ B. Phage-mediated DNA transfer
- ☐ C. Pilus-mediated DNA transfer
- ☐ D. Spontaneous DNA mutation
- ☐ E. Transposon-mediated DNA transfer





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

among different strains of *Streptococcus pneumoniae*. In the first experiment, they inject nonvirulent strain A into the peritoneal cavity of laboratory mice and observe no ill effects. In the second experiment, researchers subject virulent strain B to a detergent agent that kills and lyses the bacterial cells. They then inject the lysate into the peritoneal cavity of a new group of mice and again observe no ill effects. During a third experiment, they inject live strain A bacteria in combination with the killed strain B lysate, resulting in death of the mice. Which of the following genetic processes most likely accounts for the observed findings of these experiments?

- ☒ A. Direct uptake of extracellular DNA (73%)
- ☐ B. Phage-mediated DNA transfer (11%)
- ☐ C. Pilus-mediated DNA transfer (8%)
- ☐ D. Spontaneous DNA mutation (0%)
- ☐ E. Transposon-mediated DNA transfer (5%)

Correct

73%

Answered correctly



53 secs

Time spent



10/24/2020

Last updated

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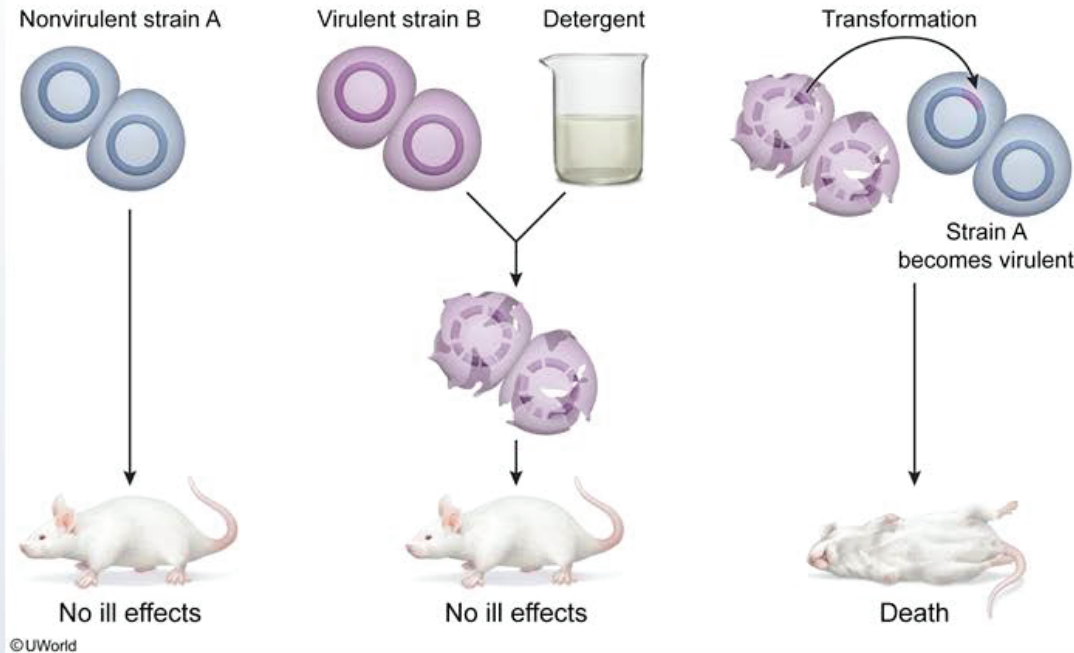


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Certain strains of *Streptococcus pneumoniae* express capsular polysaccharides that inhibit phagocytosis, making it a successful pathogen. Strains lacking the capsule are not pathogenic; however, *S pneumoniae* is able to obtain new genetic material from the environment that is released following the death and lysis of



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

Certain strains of *Streptococcus pneumoniae* express capsular polysaccharides that inhibit phagocytosis, making it a successful pathogen. Strains lacking the capsule are not pathogenic; however, *S pneumoniae* is able to obtain new genetic material from the environment that is released following the death and lysis of neighboring bacterial cells. This process, known as **transformation**, allows the bacterium to **take up exogenous DNA** fragments, integrate the DNA into its genome, and express the encoded proteins. Through this method, nonvirulent strains of *S pneumoniae* that do not form a capsule can acquire the genes that code for the capsule and therefore **gain virulence**.

Bacteria that have the innate capacity to undergo transformation are said to be naturally competent and include *Haemophilus*, *Streptococcus*, *Bacillus*, and *Neisseria* species.

**(Choice B)** In **transduction**, a bacteriophage (virus) transfers DNA from one bacterial cell to another. While replicating within a host bacterium, a bacteriophage may accidentally incorporate host bacterial DNA into the phage particle. Once released, it can then transfer DNA from the previous host into a newly infected bacterium. By this mechanism, bacteria can acquire genes for virulence and antibiotic resistance.

**(Choice C)** **Conjugation** is a form of one-way DNA transfer performed by bacteria carrying a plasmid with the fertility (F) factor. The process begins with the donating bacterium producing a sex pilus, which then forms a direct connection with the receiving bacterium. Next, the donating bacterium transfers a single



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



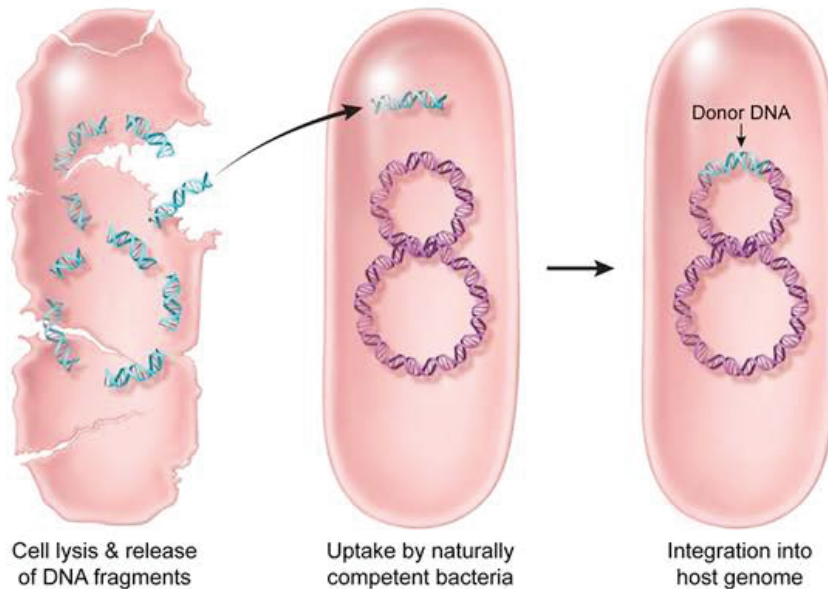
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Settings

## Exhibit Display

## Transformation



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Zoom Out



Reset



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My Notebook

Block Time Remaining: 00:26:56

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color

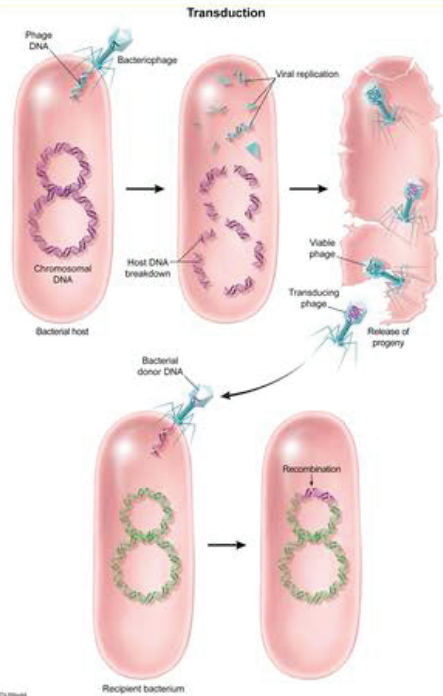


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Settings

## Exhibit Display



Zoom In



Zoom Out



Reset



New



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My Notebook



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



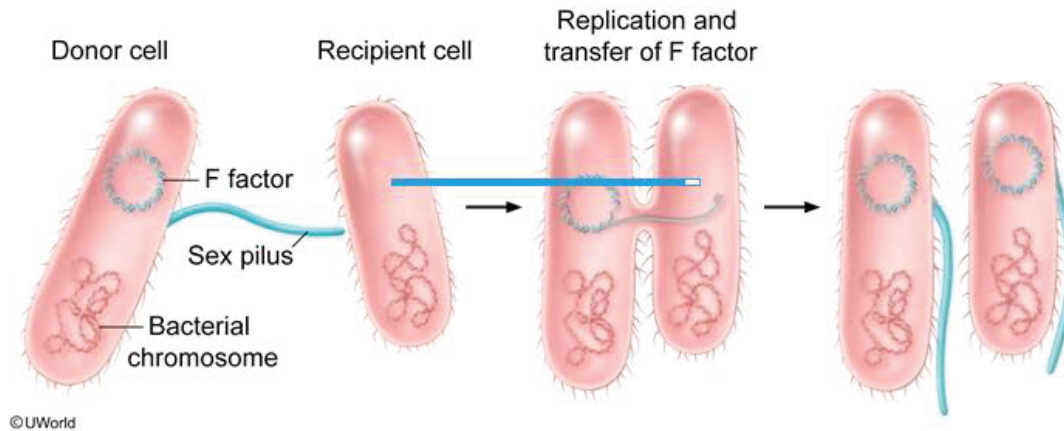
Text Zoom



Settings

## Exhibit Display

## Conjugation



Zoom In



Zoom Out



Reset



New



Existing



My Notebook



1



Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

(Choice C) Conjugation is a form of one-way DNA transfer performed by bacteria carrying a plasmid with the fertility (F) factor. The process begins with the donating bacterium producing a sex pilus, which then forms a direct connection with the receiving bacterium. Next, the donating bacterium transfers a single DNA strand containing the F factor to the recipient organism, after which, complementary DNA strands are synthesized.

(Choice D) Spontaneous or induced mutations change the nucleotide sequence of a gene, potentially altering the amino acid sequence of the protein product. Through this mechanism, bacteria form novel proteins with potentially useful functions to aid with survival.

(Choice E) Transposons are mobile genetic elements that can mediate DNA transfer from plasmids to a bacterial chromosome, move genetic material from one position to another along a bacterial chromosome, or transfer genes from a bacterial chromosome to a plasmid. The location of a gene in the genome is important as it determines its proximity to promoter or suppressor regions.

### Educational objective:

*Streptococcus pneumoniae* is able to undergo transformation, which allows the bacterium to take up exogenous DNA fragments and express the encoded proteins. Through this method, strains of *S pneumoniae* that do not form a capsule can acquire the genes that code for the capsule and therefore gain virulence.



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Feedback

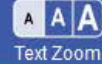
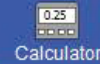
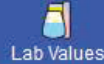
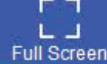


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A 36-year-old man comes to the office due to 2 months of fatigue, intermittent arthralgias, and poor appetite. The patient has no prior medical conditions and takes no medications. He does not use tobacco or illicit drugs, and he drinks alcohol occasionally. The patient has had multiple sexual partners and uses condoms inconsistently. Physical examination shows no abnormalities. Liver aminotransferases are elevated. Hepatitis serology shows the following:

Hepatitis A virus antibody, total	negative
Hepatitis B surface antibody (HBsAb)	negative
Hepatitis B core antibody (HBcAb), total	positive
Hepatitis B surface antigen (HBsAg)	positive
Hepatitis B E antigen (HBeAg)	positive
Hepatitis C virus antibody	negative

Which of the following genome replicative processes is most likely used by the virus infecting this patient?

- ☐ A. Double-stranded DNA → double-stranded DNA template → double-stranded DNA progeny





Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Hepatitis B surface antigen (HBsAg) positive

Hepatitis B E antigen (HBeAg) positive

Hepatitis C virus antibody negative

Which of the following genome replicative processes is most likely used by the virus infecting this patient?

- ☐ A. Double-stranded DNA → double-stranded DNA template → double-stranded DNA progeny
- ☐ B. Double-stranded DNA → +RNA template → partially double-stranded DNA progeny
- ☐ C. Single-stranded DNA → double-stranded DNA template → single-stranded DNA progeny
- ☐ D. Single-stranded +RNA → double-stranded DNA template → single-stranded +RNA progeny
- ☐ E. Single-stranded +RNA → -RNA template → single-stranded +RNA progeny
- ☐ F. Single-stranded -RNA → +RNA template → single-stranded -RNA progeny

**Submit**

Block Time Remaining: 00:27:01

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Hepatitis B core antibody (HBcAb), total	positive
Hepatitis B surface antigen (HBsAg)	positive
Hepatitis B E antigen (HBeAg)	positive
Hepatitis C virus antibody	negative

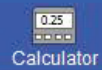
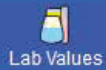
Which of the following genome replicative processes is most likely used by the virus infecting this patient?

- ☐ A. Double-stranded DNA → double-stranded DNA template → double-stranded DNA progeny (16%)
- ☒ B. Double-stranded DNA → +RNA template → partially double-stranded DNA progeny (67%)
- ☐ C. Single-stranded DNA → double-stranded DNA template → single-stranded DNA progeny (6%)
- ☐ D. Single-stranded +RNA → double-stranded DNA template → single-stranded +RNA progeny (6%)
- ☐ E. Single-stranded +RNA → -RNA template → single-stranded +RNA progeny (2%)
- ☐ F. Single-stranded -RNA → +RNA template → single-stranded -RNA progeny (1%)



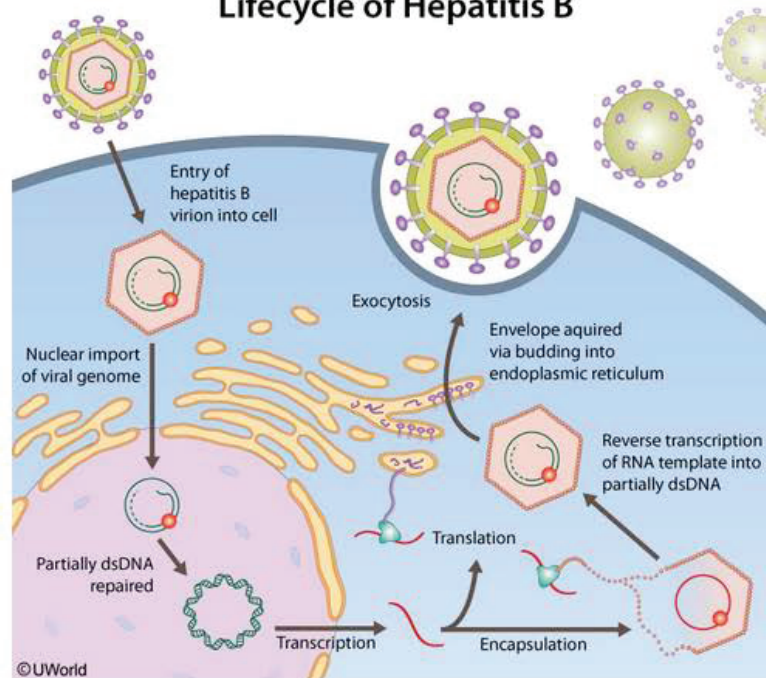
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## Exhibit Display

## Lifecycle of Hepatitis B



Zoom In Zoom Out Reset New Existing My Notebook

Block Time Remaining: 00:27:30

<https://t.me/USMLEWorldStep1>





Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

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**Acute hepatitis B virus (HBV)** infection is marked by the presence of HBsAg, HBeAg, and anti-HBc, and a lack of anti-HBs. Infections are often asymptomatic, but many patients have a few months of jaundice, fatigue, nausea, and right upper-quadrant discomfort. Perinatal transmission is most common in high-prevalence countries (eg, Sub-Saharan Africa); in low-prevalence regions (eg, United States), most cases occur due to unprotected sex or intravenous drug use.

HBV is a hepadnavirus composed of:

- an **outer lipid envelope** that contains viral-encoded proteins (HBsAg) and host lipid components.
- an **icosahedral nucleocapsid core** that contains a circular, partially double-stranded DNA genome and a DNA polymerase with reverse transcriptase activity.

HBV binds to a bile salt transporter on the surface of hepatocytes and enters the cell. After the virus is uncoated in the host cytoplasm, the single-stranded DNA portion of the viral genome is completed (repaired) by cellular DNA polymerases. This generates **double-stranded viral DNA**, which is subsequently transcribed by host RNA polymerase into a **+single-stranded RNA pregenome**. The +RNA template is then translated into the proteins that compose the virus (eg, envelope, core, polymerase); it is also converted by viral DNA polymerase/reverse transcriptase into the **partially double-stranded DNA**.

Block Time Remaining: 00:27:30

<https://t.me/USMLEWorldStep1>

Feedback

Suspend

End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

subsequently transcribed by host RNA polymerase into a **+single-stranded RNA pregenome**. The +RNA template is then translated into the proteins that compose the virus (eg, envelope, core, polymerase); it is also converted by viral DNA polymerase/reverse transcriptase into the **partially double-stranded DNA progeny** of developing viral particles.

**(Choice A)** This replicative sequence characterizes adenovirus, herpesvirus, and poxvirus.

**(Choice C)** This replicative sequence characterizes parvovirus B19.

**(Choice D)** This replicative sequence characterizes the retroviruses (eg, HIV).

**(Choice E)** This replicative sequence characterizes poliovirus.

**(Choice F)** This replicative sequence characterizes influenza virus, measles virus, and rabies virus.

### Educational objective:

The hepatitis B virus (HBV) replicates via the following sequence: double-stranded DNA → +RNA template → partially double-stranded DNA progeny. Although it is a DNA virus, HBV uses reverse transcription to generate new viral DNA from a positive-sense RNA template.

Microbiology

Microbiology (General Principles)

Hepatitis b

Block Time Remaining: 00:27:30

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



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5

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24

25

26

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28

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Item 28 of 31

Question Id: 1485



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

*E. coli* colonies grown on a lactose-containing medium up-regulate the production of the enzymes  $\beta$ -galactosidase and galactoside permease. Which of the following best explains the synchronous production of both enzymes in response to lactose?

- ☐ A. There are two activator binding sites for one activator protein
- ☐ B. There are two operators for one repressor protein
- ☐ C. There are two repressors for one inducer
- ☐ D. There are two promoters in close proximity to each other
- ☐ E. There is one mRNA coding for both enzymes

**Submit**

Block Time Remaining: 00:27:31

<https://t.me/USMLEWorldStep1>

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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom




Settings

*E. coli* colonies grown on a lactose-containing medium up-regulate the production of the enzymes  $\beta$ -galactosidase and galactoside permease. Which of the following best explains the synchronous production of both enzymes in response to lactose?

- ☐ A. There are two activator binding sites for one activator protein (11%)
- ☐ B. There are two operators for one repressor protein (13%)
- ☐ C. There are two repressors for one inducer (4%)
- ☐ D. There are two promoters in close proximity to each other (14%)
- ☒ E. There is one mRNA coding for both enzymes (55%)

Correct

 55%  
Answered correctly 47 secs  
Time Spent 01/30/2021  
Last Updated

Explanation

Block Time Remaining: 00:28:17

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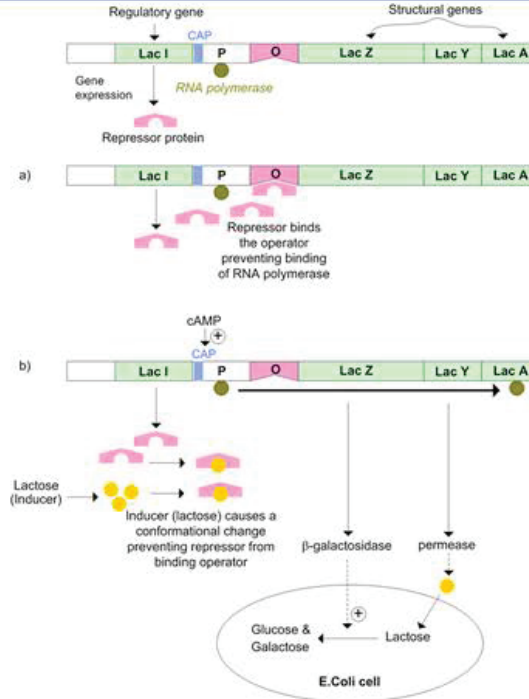


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End Block

### Exhibit Display







Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

The *lac* operon is the sequence of the *E. coli* genome which is required for the metabolism of lactose. The *lac* operon consists of a regulatory gene (*i*), promoter region (*p*), operator region (*o*), and three structural genes (*z*, *y*, and *a*). The *z* gene codes for  $\beta$ -galactosidase ( $\beta$ -gal), which is primarily responsible for the hydrolysis of lactose to glucose and galactose. The *y* gene codes for permease, a transmembrane enzyme that increases the permeability of the cell to lactose. The *a* gene encodes a  $\beta$ -galactoside transacetylase, which transfers acetyl groups to  $\beta$ -galactosides and is unnecessary for lactose metabolism by *E. coli*.

In prokaryotes, one mRNA transcript contains the sequences for many proteins, and a single mRNA molecule can be translated into multiple proteins or polypeptides. For instance, all three proteins of the *lac* operon ( $\beta$ -galactosidase, permease, and transacetylase) are synthesized from a single mRNA molecule containing the *z*, *y*, and *a* gene sequences, respectively. Transcription and translation of the genes of the *lac* operon is typically synchronous. Remember that a single mRNA molecule which codes for more than one protein is referred to as a polycistronic mRNA, and while most prokaryotic mRNA molecules are polycistronic, eukaryotic mRNA is rarely polycistronic.

**(Choices A – D)** The *lac* operon, which codes for all three aforementioned proteins, is regulated by a single operator, a promoter, and a single group of regulatory elements: an inducer, repressor, and catabolite activator protein. Modulation of the transcription of this operon through binding of the operator



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Feedback



Suspend



End Block



Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



Calculator



Reverse Color



Text Zoom



Settings

polycistronic, eukaryotic mRNA is rarely polycistronic.

**(Choices A – D)** The lac operon, which codes for all three aforementioned proteins, is regulated by a single operator, a promoter, and a single group of regulatory elements: an inducer, repressor, and catabolite activator protein. Modulation of the transcription of this operon through binding of the operator and action of the repressor or other regulatory elements will change the transcription of all three *lac*-operon structural genes (*z*, *y*, and *a*). On the other hand, there are no operators, repressors, or inducers that can desynchronize the transcription of lac-operon structural genes.

### Educational Objective:

Bacterial mRNA can be polycistronic, meaning that one mRNA codes for several proteins. An example of polycistronic mRNA is the bacterial lac operon, which codes for the proteins necessary for lactose metabolism by *E. coli*; the transcription and translation of these bacterial proteins is regulated by a single promoter, operator, and set of regulatory elements.

Microbiology  
Subject

Microbiology (General Principles)  
System

Lac operon  
Topic

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Block Time Remaining: 00:28:17

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Feedback



Suspend



End Block

5

6

7

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9

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13

14

15

16

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18

19

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21

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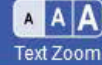
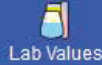
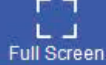
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A 25-year-old woman comes to the emergency department due to 2 days of abdominal pain and bloody diarrhea. A few days ago, she attended a church barbeque party. The patient lives alone and has no medical problems. She does not know if anyone else at the party developed similar symptoms. Her temperature is 37.1 C (98.8 F), blood pressure is 119/76 mm Hg, pulse is 92/min, and respirations are 16/min. There is abdominal tenderness with no rebound or guarding. Guaiac-positive bloody stools are detected on rectal examination. Stool cultures reveal an *Escherichia coli* strain that does not produce glucuronidase and does not ferment sorbitol on sorbitol-containing MacConkey agar. Which of the following best describes the mechanism of action of the toxin produced by these bacteria?

- ☐ A. Activates adenylate cyclase
- ☒ B. Activates guanylate cyclase
- ☐ C. Disrupts the cellular cytoskeleton
- ☐ D. Inactivates elongation factor-2
- ☐ E. Inactivates ribosomal subunits





diarrhea. A few days ago, she attended a church barbeque party. The patient lives alone and has no medical problems. She does not know if anyone else at the party developed similar symptoms. Her temperature is 37.1 C (98.8 F), blood pressure is 119/76 mm Hg, pulse is 92/min, and respirations are 16/min. There is abdominal tenderness with no rebound or guarding. Guaiac-positive bloody stools are detected on rectal examination. Stool cultures reveal an *Escherichia coli* strain that does not produce glucuronidase and does not ferment sorbitol on sorbitol-containing MacConkey agar. Which of the following best describes the mechanism of action of the toxin produced by these bacteria?

- ☐ A. Activates adenylate cyclase (14%)
- ☐ B. Activates guanylate cyclase (8%)
- ☐ C. Disrupts the cellular cytoskeleton (12%)
- ☐ D. Inactivates elongation factor-2 (11%)
- ✓ ☒ E. Inactivates ribosomal subunits (53%)

Correct

53%

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### Mechanism of action of selected bacterial exotoxins

Organism	Toxin	Mechanism & effects
<i>Bacillus anthracis</i>	Anthrax exotoxin	Edema factor: Increases cyclic AMP concentration by acting as an adenylate cyclase, causing edema & phagocyte dysfunction
		Lethal factor: Zinc-dependent protease that inhibits mitogen-activated protein kinase signaling, causing apoptosis & multisystem physiologic disruption
<i>Bordetella pertussis</i>	Pertussis toxin	Disinhibits adenylate cyclase through G <sub>i</sub> ADP-ribosylation, increasing cAMP levels; causes edema & phagocyte dysfunction
	Adenylate cyclase toxin	Functions as an adenylate cyclase, increasing cAMP levels; causes edema & phagocyte dysfunction
<i>Clostridium botulinum</i>	Botulinum toxin	Blocks presynaptic release of acetylcholine at the neuromuscular junction, resulting in flaccid paralysis

<i>Clostridium difficile</i>	Toxin A	Recruits & activates neutrophils, leading to release of cytokines that cause mucosal inflammation, fluid loss & diarrhea
	Toxin B	Induces actin depolymerization, leading to mucosal cell death, bowel wall necrosis & pseudomembrane formation
<i>Shigella dysenteriae</i>	Shiga toxin	Halts protein synthesis by disabling the 60S ribosomal subunit, leading to intestinal epithelial cell death & diarrhea
<i>Streptococcus pyogenes</i>	Pyrogenic exotoxin	Acts as a superantigen, inducing fever & shock; associated with scarlet fever & streptococcal toxic shock syndrome
	Streptolysin O&S	Damages erythrocyte membranes, causing beta hemolysis

**Enterohemorrhagic *Escherichia coli* (EHEC) O157:H7** can cause hemorrhagic colitis, most characteristically following ingestion of inadequately cooked hamburger meat. In contrast to most *E coli* strains, O157:H7 *E coli* does **not** ferment sorbitol during overnight incubation. As a result, sorbitol-containing MacConkey agar is used for isolation. Also, unlike other *E coli* strains, *E coli* O157:H7 does **not** produce glucuronidase.





Mark



Previous



Next



Full Screen



Tutorial



Lab Values



Notes



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Settings

produce glucuronidase.

EHEC elaborates a **Shiga-like toxin** virtually identical to the Shiga toxin produced by *Shigella dysenteriae*. This toxin is phage encoded, and its production is enhanced by iron deficiency. The Shiga and the Shiga-like toxins inactivate the 60s **ribosomal subunit** in human cells, leading to an inhibition of protein synthesis and eventual cell death. Infection with EHEC can also lead to hemolytic-uremic syndrome, characterized by thrombocytopenia, microangiopathic hemolytic anemia, and renal insufficiency (sometimes with uremia).

Unlike enteroinvasive *E coli*, EHEC does not invade the intestinal mucosa. Unlike enterotoxigenic *E coli* (ETEC), EHEC does not produce heat-labile toxin (LT) or heat-stable toxin (ST).

**(Choice A)** Toxins produced by *Bordetella pertussis* (adenylate cyclase toxin), ETEC (LT), *Campylobacter jejuni* (*C jejuni* enterotoxin), and *Vibrio cholerae* (cholera toxin) result in increased intracellular cyclic AMP in intestinal mucosal cells, which leads to decreased absorption and increased secretion of sodium, chloride, and water.

**(Choice B)** ETEC (ST) and *Yersinia enterocolitica* (*Y enterocolitica* enterotoxin) produce toxins that increase intracellular cyclic GMP, leading to watery diarrhea and electrolyte loss.

**(Choice C)** *Clostridium difficile* produces an exotoxin capable of disrupting the cytoskeleton (toxin B/exfoliatin). This toxin acts by depolymerizing actin, leading to cell death.

Block Time Remaining: 00:29:55

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*jejuni* (*C jejuni* enterotoxin), and *Vibrio cholerae* (cholera toxin) result in increased intracellular cyclic AMP in intestinal mucosal cells, which leads to decreased absorption and increased secretion of sodium, chloride, and water.

**(Choice B)** ETEC (ST) and *Yersinia enterocolitica* (*Y enterocolitica* enterotoxin) produce toxins that increase intracellular cyclic GMP, leading to watery diarrhea and electrolyte loss.

**(Choice C)** *Clostridium difficile* produces an exotoxin capable of disrupting the cytoskeleton (toxin B/cytotoxin). This toxin acts by depolymerizing actin, leading to cell death.

**(Choice D)** Exotoxins produced by *Corynebacterium diphtheriae* (diphtheria toxin) inhibit protein synthesis in eukaryotic cells by catalyzing ADP-ribosylation of elongation factor (EF)-2, causing EF-2 inactivation.

**Educational objective:**

Enterohemorrhagic *Escherichia coli* O157:H7 infection is a common cause of bloody diarrhea and can lead to hemolytic-uremic syndrome. It is associated with consumption of undercooked ground beef and elaborates a Shiga-like toxin capable of inhibiting protein synthesis in colonic mucosal cells and renal endothelial cells. This particular strain of *E coli* is unable to ferment sorbitol and does not produce a glucuronidase.

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A 22-year-old woman comes to the emergency department due to intermittent fevers and chills over the past few days. Last week, she underwent routine dental cleaning with no complications. The patient has a history of mitral valve prolapse. Temperature is 38.2 C (100.8 F). Physical examination reveals a non-ejection mid-systolic click followed by a late-systolic murmur best heard at the cardiac apex. Blood cultures are drawn and grow gram-positive bacteria that synthesize dextran from sucrose. Which of the following would be the most likely adherence site for these bacteria?

- ☐ A. Circulating heparins
- ☐ B. Endothelial surface glycoproteins
- ☐ C. Fibrin-platelet aggregates
- ☐ D. Subendothelial collagen
- ☐ E. Subendothelial glycosaminoglycans

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Previous



Next



Full Screen



Tutorial



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Notes



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A 22-year-old woman comes to the emergency department due to intermittent fevers and chills over the past few days. Last week, she underwent routine dental cleaning with no complications. The patient has a history of mitral valve prolapse. Temperature is 38.2 C (100.8 F). Physical examination reveals a non-ejection mid-systolic click followed by a late-systolic murmur best heard at the cardiac apex. Blood cultures are drawn and grow gram-positive bacteria that synthesize dextrans from sucrose. Which of the following would be the most likely adherence site for these bacteria?

- ☐ A. Circulating heparins (0%)
- ☐ B. Endothelial surface glycoproteins (24%)
- ☒ C. Fibrin-platelet aggregates (53%)
- ☐ D. Subendothelial collagen (10%)
- ☐ E. Subendothelial glycosaminoglycans (11%)

Correct

 53%  
Answered correctly 01 min, 05 secs  
Time Spent 11/15/2020  
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Block Time Remaining: 00:31:00

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Feedback



Suspend



End Block



Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

This patient with mitral valve prolapse (as suggested by the auscultated systolic click and murmur) now has bacteremia following dental cleaning. **Viridans streptococci** are normal inhabitants of the oral cavity and cause **transient bacteremia** after **dental** procedures. These gram-positive organisms are capable of producing extracellular polysaccharides (**dextrans**) using sucrose as a substrate.

Dextrans facilitate streptococcal adherence to fibrin. **Fibrin and platelets** are deposited at sites of endothelial trauma, providing a site for bacterial adherence and colonization during bacteremia. In patients with pre-existing valvular lesions, viridans streptococci can adhere to the affected valve and establish infection leading to endocarditis. Other factors that facilitate pathogenesis may also be involved. *Staphylococcus aureus* is more aggressive and can adhere to intact valves. The risk of endocarditis following dental procedures is low with mitral valve prolapse, and antibiotic prophylaxis is not recommended; however, cases can still occur.

**(Choice A)** Circulating heparins prolong the partial thromboplastin time by activating antithrombin III, thereby decreasing thrombin activity and ultimately preventing fibrinogen conversion to fibrin, thereby preventing clot formation. Circulating heparins would not provide a binding site for bacteria.

**(Choice B)** Endothelial surface glycoproteins mediate binding of immune cells to endothelium, facilitated by the expression of cell adhesion molecules on the surface of inflamed endothelium. Neutrophils are then



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**(Choice B)** Endothelial surface glycoproteins mediate binding of immune cells to endothelium, facilitated by the expression of cell adhesion molecules on the surface of inflamed endothelium. Neutrophils are then able to bind and migrate between the endothelial cells, followed by monocytes and lymphocytes.

**(Choices D and E)** Subendothelial collagen and glycosaminoglycans form the subendothelial fibrous cap over the central core of an atherosclerotic plaque and are potent platelet activators. When exposed (eg, denuded endothelium in atherosclerotic plaque), they contribute to rapid thrombus formation that can lead to myocardial infarction in a coronary artery.

**Educational objective:**

Viridans streptococci are normal inhabitants of the oral cavity and are a cause of transient bacteremia after dental procedures in healthy and diseased individuals. In patients with pre-existing valvular lesions, viridans streptococci can adhere to fibrin-platelet aggregates and establish infection that leads to endocarditis.

Microbiology	Microbiology (General Principles)	Endocarditis
Subject	System	Topic

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Researchers are studying mechanisms of human infection by animal viruses. The investigators induce random mutations in the genome of an avian influenza virus that is unable to infect humans but is structurally similar to human influenza A virus. A mutated isolate is found to be able to infect human upper respiratory tract epithelial cells. Alteration in which of the following viral components most likely enabled this novel strain to cause cross-species infection?

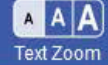
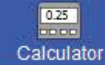
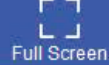
- ☐ A. Antigenic glycoprotein
- ☐ B. Lipid bilayer envelope
- ☐ C. mRNA endonuclease
- ☐ D. Nucleocapsid protein
- ☐ E. RNA polymerase

**Submit**

Researchers are studying mechanisms of human infection by animal viruses. The investigators induce random mutations in the genome of an avian influenza virus that is unable to infect humans but is structurally similar to human influenza A virus. A mutated isolate is found to be able to infect human upper respiratory tract epithelial cells. Alteration in which of the following viral components most likely enabled this novel strain to cause cross-species infection?

- ☒ A. Antigenic glycoprotein (57%)
- ☐ B. Lipid bilayer envelope (8%)
- ☒ C. mRNA endonuclease (4%)
- ☐ D. Nucleocapsid protein (24%)
- ☐ E. RNA polymerase (5%)

**Incorrect**Correct answer  
A 57%  
Answered correctly 01 min, 05 secs  
Time Spent 11/28/2020  
Last Updated



**Influenza virus** is a segmented, negative-sense RNA virus that is enveloped within a host-derived plasma membrane. Interaction with the host cell is dependent upon a viral **surface glycoprotein** called **hemagglutinin**, which binds to the sialic acid receptor on human respiratory epithelial cells. Influenza strains that are unable to infect humans (eg, avian/swine influenza) encode for hemagglutinin that cannot bind to human cells.

However, influenza is prone to **antigenic changes** in its surface glycoproteins due to:

- Poor proofreading of viral RNA-dependent RNA polymerase, which results in the introduction of genetic mutations during replication (antigenic drift).
- Reassortment of the segmented genome when 2 influenza viruses infect the same cell, which results in dramatic alterations to the genome (antigenic shift).

Antigenic changes to hemagglutinin can alter the **tissue tropism** of the virus and allow strains that previously only affected livestock (eg, avian, swine) to infect human cells.

**(Choice B)** The influenza lipid bilayer envelope is generated from host cells during viral replication. Because it is composed of host cell lipids, it is unlikely to be significantly altered by viral mutations.

**(Choices C, D, and E)** Following **influenza attachment** and endocytosis, the viral bilayer envelope fuses







Mark

Previous

Next

Full Screen

Tutorial

Lab Values

Notes

Calculator

Reverse Color

Text Zoom

Settings

Antigenic changes to hemagglutinin can alter the **tissue tropism** of the virus and allow strains that previously only affected livestock (eg, avian, swine) to infect human cells.

**(Choice B)** The influenza lipid bilayer envelope is generated from host cells during viral replication. Because it is composed of host cell lipids, it is unlikely to be significantly altered by viral mutations.

**(Choices C, D, and E)** Following **influenza attachment** and endocytosis, the viral bilayer envelope fuses with the endosome membrane, which liberates the nucleocapsid protein (bound to the RNA genome), viral RNA-dependent RNA polymerase, and viral mRNA endonuclease into the cytoplasm. These travel to the nucleus to initiate viral replication. Although mutations to these proteins could affect viral replication, they would be unlikely to alter tissue tropism because they are not on the surface of the virus and, therefore, do not mediate viral attachment.

### Educational objective:

The tissue tropism of viruses is primarily mediated by viral surface glycoproteins that bind to specific host cell receptors. Mutations to viral surface glycoproteins can alter tissue tropism and cause noninfective viruses to become infectious.

Microbiology

Microbiology (General Principles)

Influenza

Subject

System

Topic

Block Time Remaining: 00:32:05

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Antigenic changes to hemagglutinin can alter the tissue tropism of the virus and allow strains that

### Exhibit Display

